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An overview of the models available for simulating human food digestion : mythe or reality?

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HAL Authorization

An overview of the models available for simulating human food digestion: myth or reality?



STLOpen Days
19-21 March 2019



Olivia Menard - STLO



Context

2 key words :

« **In vitro** digestion » and « foods »

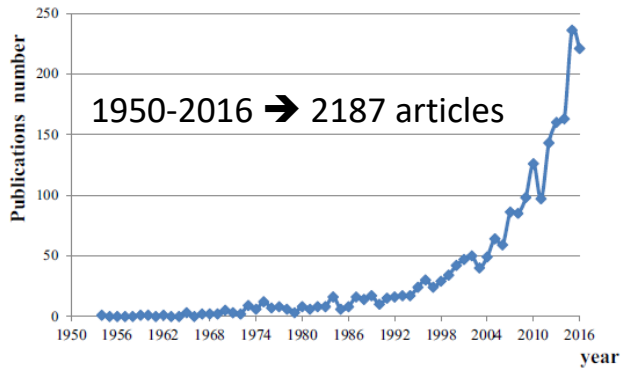
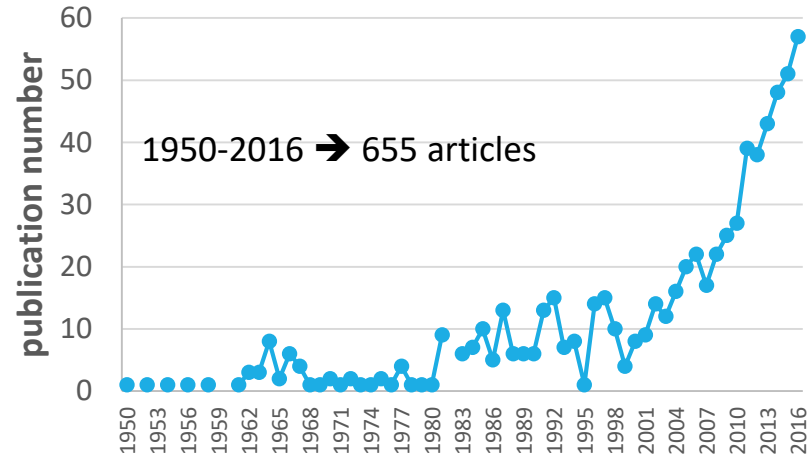


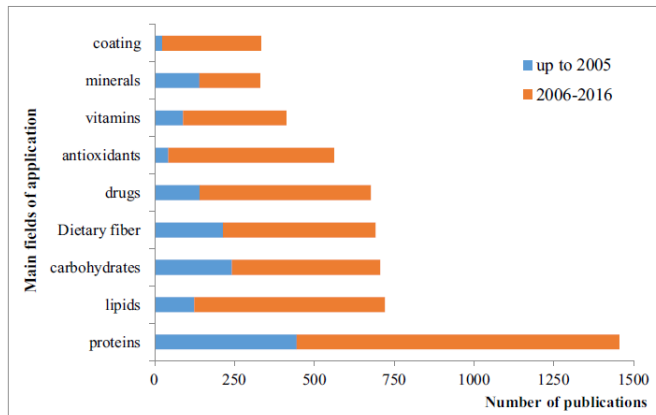
Fig. 2. Evolution of the number of publications on *in vitro* digestion studies.

2 key words :

« **In vivo** digestion » and « foods »

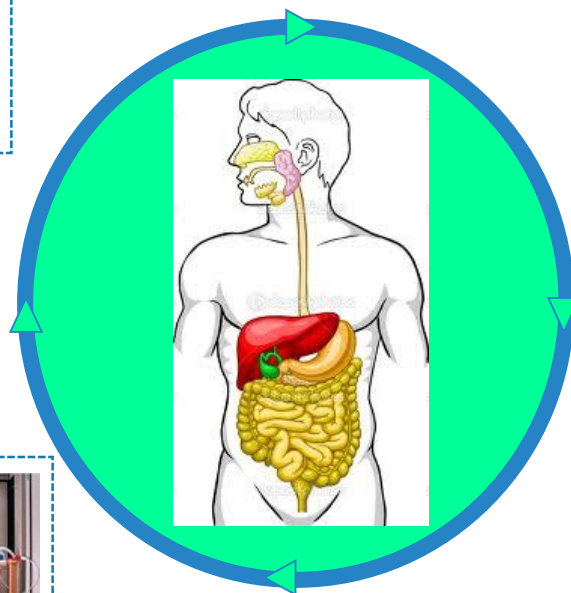


Lucas-Gonzales et al, FRI; 2018



How to study digestion : from *in vivo* to *in vitro*

In vitro
static models



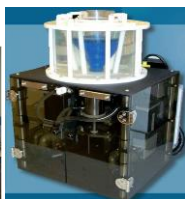
In vivo
Clinical studies



In vivo
Animal models
(rats, pigs, mini-pigs, piglets...)



In vitro
Dynamic models



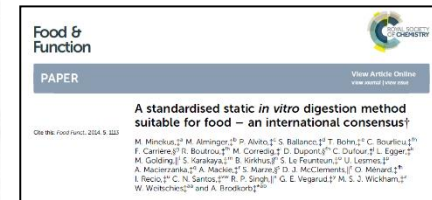
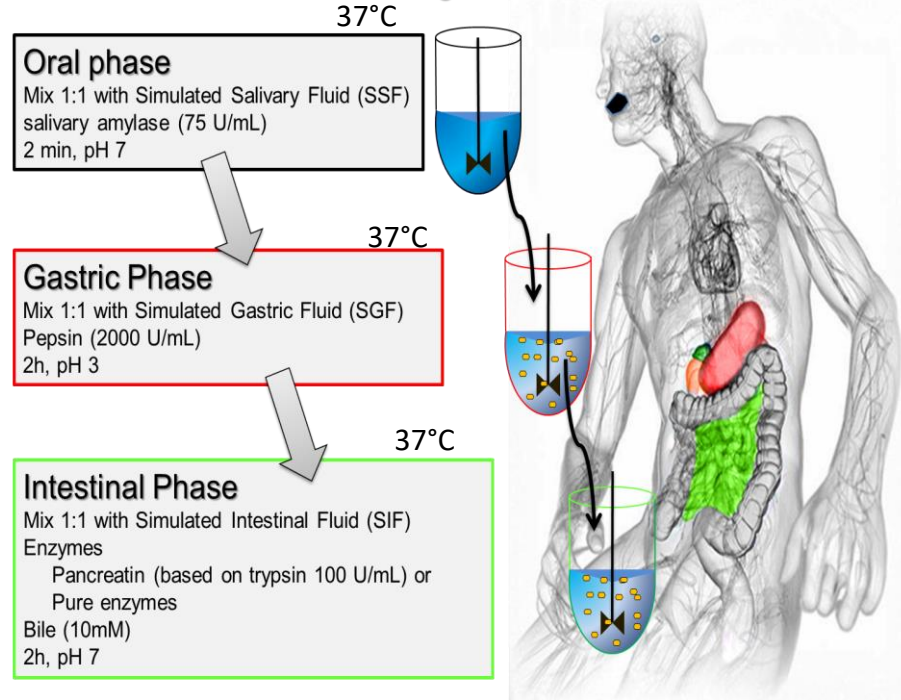
Static *in vitro* digestion models adapted for adults

- ☞ 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

INFOGEST

International network
 – 400 researchers
 – 140 institutes
 – 43 countries

Consensus *in vitro* digestion method for food



Updated version accepted for publication
 Nature Protocols (IF=15.269)

Minekus et al; 2014
Highly Cited Paper 897 citations in less than 5 years

Static *in vitro* digestion models adapted for infants

Objective:
Simulate the immaturity of the newborn digestive tract



Infant



No oral phase

Gastric phase

Ratio Meal : Simulated Gastric Fluid of **63:37**

Enzymes : Pepsin (**268 U/mL**) and Lipase (**21 U/mL**) from **Rabbit Gastric Extract**

60 min of digestion at pH 5.3

37°C

Intestinal phase

Ratio meal : Simulated Gastric Fluid of **39:61**

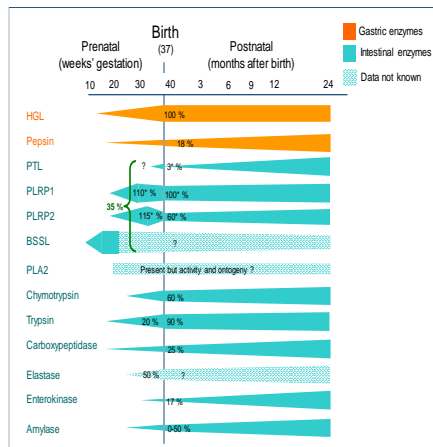
Enzymes: porcine pancreatin (lipase : **90 U/mL**)

Bovine bile (3.1 mmol/L)

60 min of digestion at pH 6.6

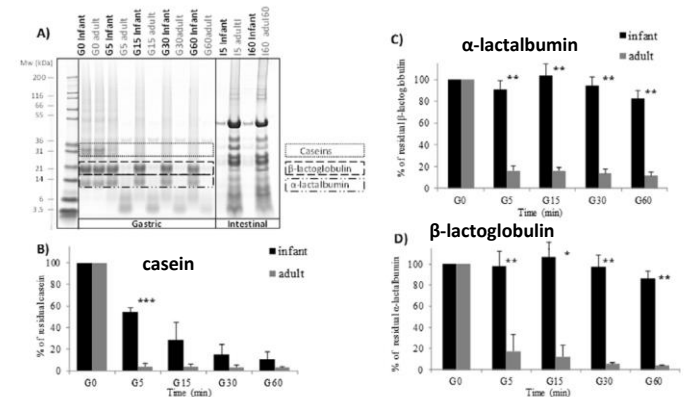
37°C

Enzyme ontogenesis



Bourlieu et al., 2014

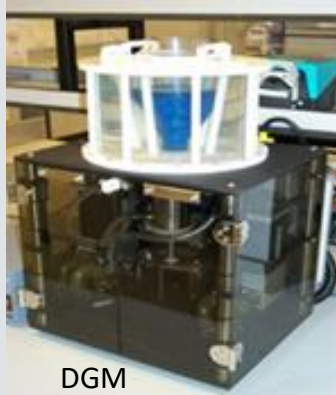
Comparison of proteolysis
adults vs infants
gastric conditions



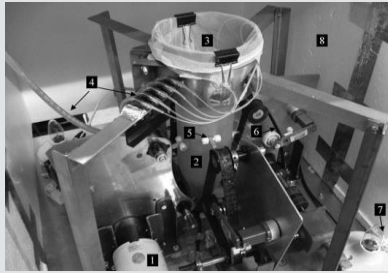
→ lower proteolysis in infant gastric conditions

Menard et al; Food Chem, 2018

Dynamic *in vitro* digestion models

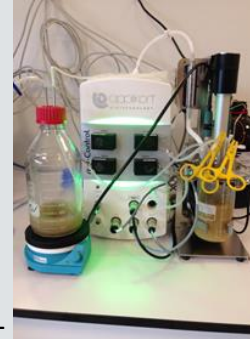


DGM
(stomach)

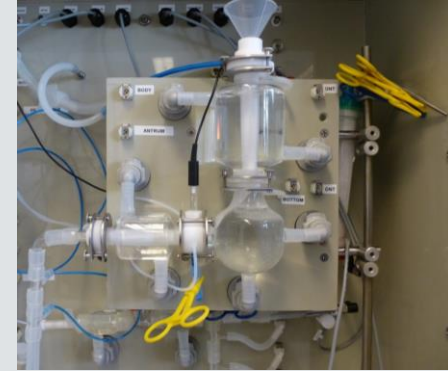


HGS
(stomach)

Mono-compartmental models



ARCOL
(colon)



Advanced Gastric Compartment
(AGC) TNO

DIDGI (stomach + small intestine)



Multi-compartmental models

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



ESIN
(stomach +
small
intestine)



SIMGI (whole GI tract)



SHIME (whole GI tract)

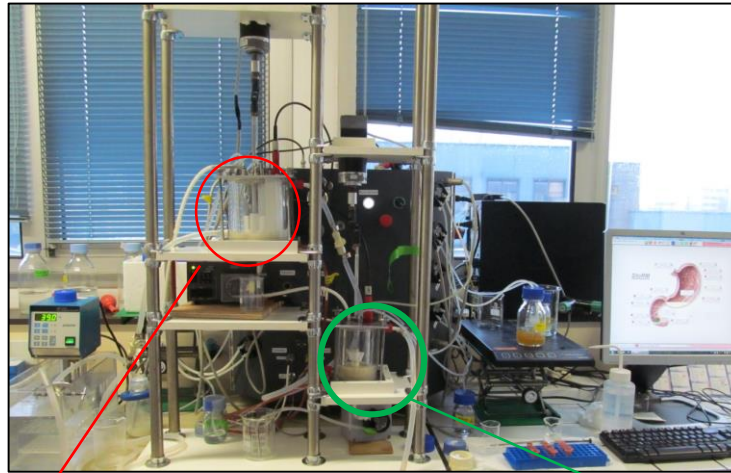


Dupont et al. 2017

DIGESTEUR DYNAMIQUE GASTRO-INTESTINAL

5 DIDGi
in different research
units of INRA

DIDGI®
Dynamic Digester
Gastro-intestinal



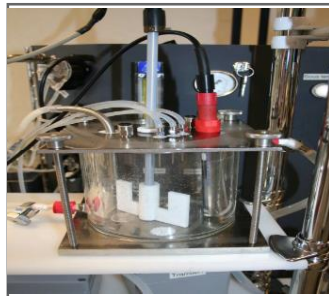
Software : STORM®
(STOMach Regulation
and Monitoring)



Stomach

Intestine

Gastric fluids:
- simulated gastric
fluids (electrolytes)
- pepsin
- lipase
- HCl



Gastric emptying :
Modelisation from
Elashoff equation



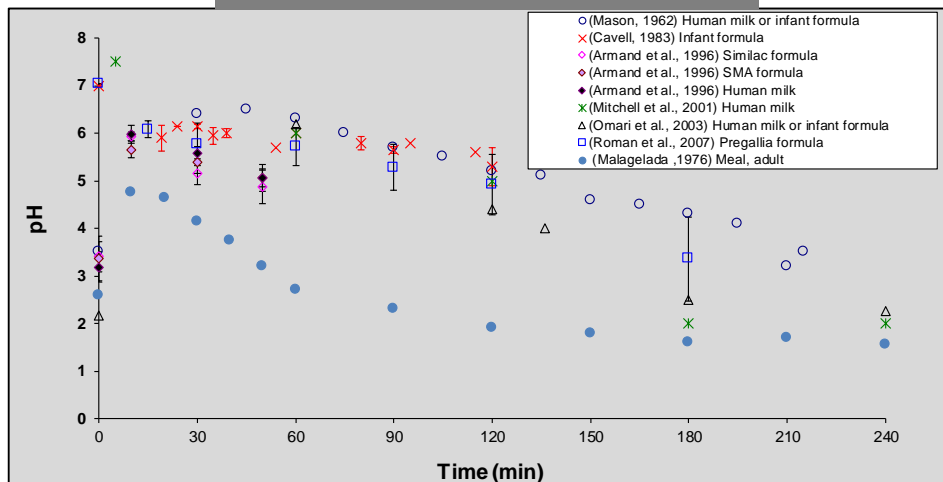
Intestinal fluids:
- simulated Intestinal
fluid (electrolytes)
- pancreatin
- bile
- NaHCO₃

Intestinal emptying :
Modelisation
(Elashoff)

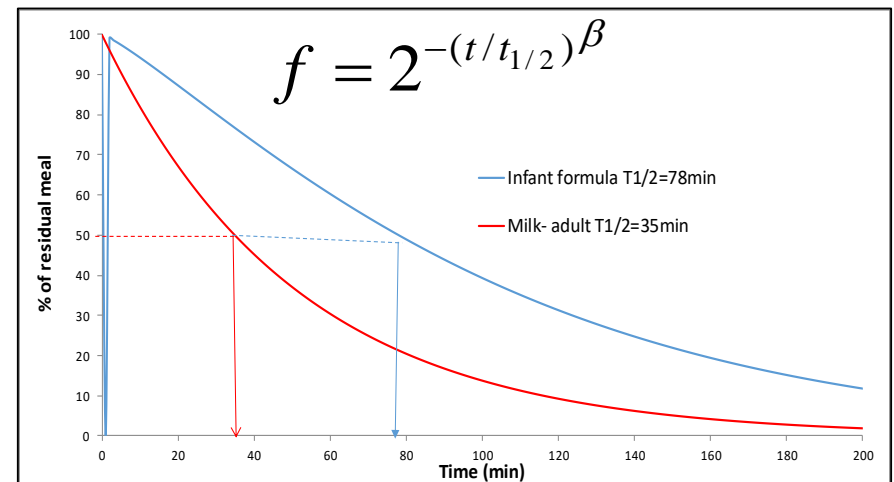
Need parameters to set up the simulator

- Parameters taken from previous *in vivo* studies

Gastric acidification curve



Gastric emptying rate

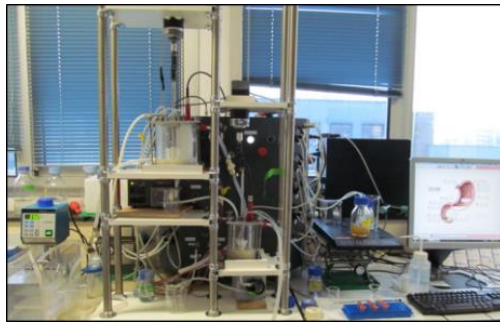


- In vivo data are crucial to set up simulators and be relevant: **key point**

Elashoff et al, 1982

f : residual volume
 $t_{1/2}$ (min) = half time emptying
 β : coefficient describing the shape of the curve

Validation of the dynamic *in vitro* digestion system

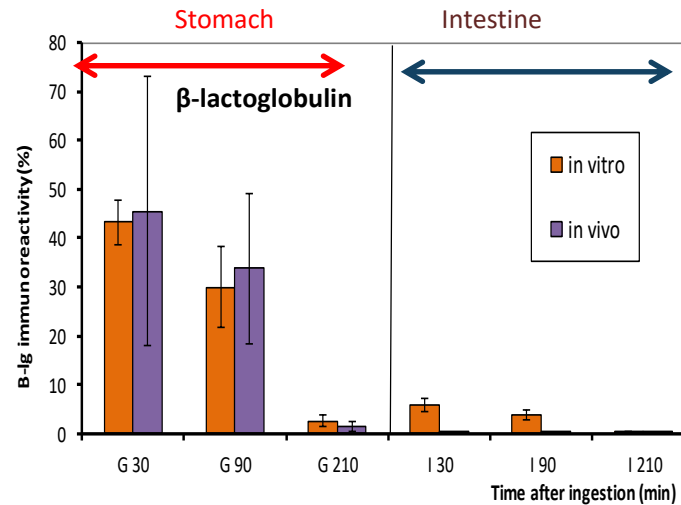
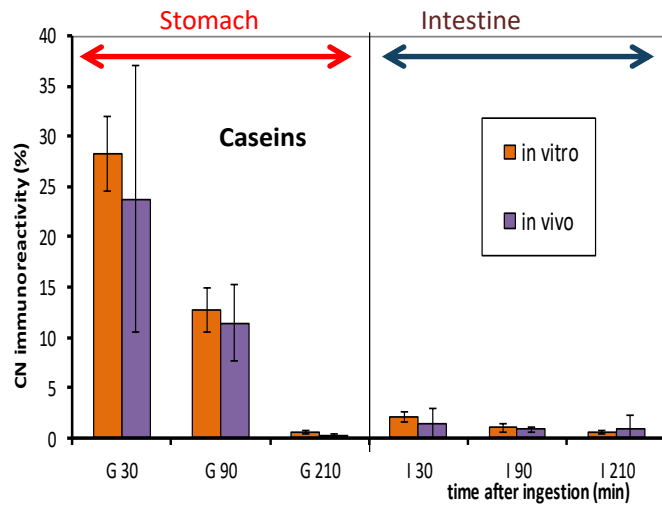


In vitro
←
N=3

Infant Formula



In vivo
→
18 piglets

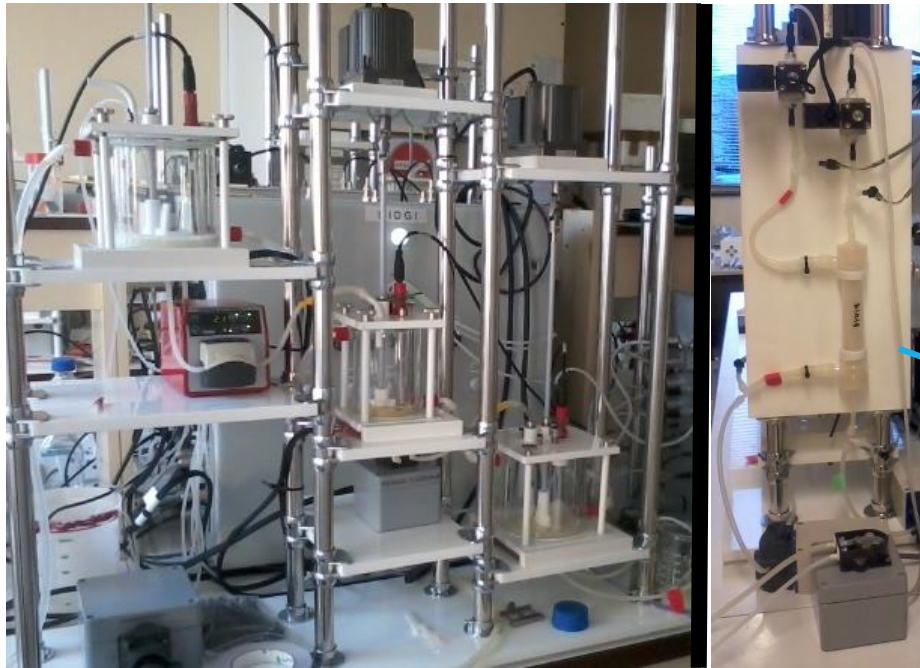


Validation:
 → proteolysis kinetic
 → residual gastric volume

Menard et al, Food chem; 2014

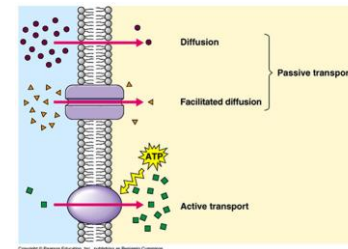
PERPECTIVE: NEW DIDGI

DiDGI version 1 used since 8 years new improvements are needed



Objective:

- Mimic the intestinal absorption



↓
Dialysis fibers to simulate
nutrient absorption from the
intestinal bowl

Digestion *in vitro* models: pro's & con's



- Standardisation of the experimental conditions
- Good reproducibility and repeatability
- Low cost, less time consuming
- Usefull for screening different foods

Static

+

Physiology relevance



- Difficult to mimic the complexity of the GI tract in a test tube!!!
(no transit, no secretion flows..)

- Highly reproducible
- Robust system
- Physiologically relevant
(in vivo data needed to adjust parameters)
- Flow of enzymes and transit

Dynamic +++

- More expensive than static models
- Too « large » to use pure enzymes
(gastric lipase)
- Few instruments available
- No nervous or hormonal control/feedback

Bohn et al. 2017 Crit Rev Food Sci Nutr
Dupont et al. 2018 Crit Rev Food Sci Nutr

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



Le Huerou-Luron et al.
2016 Eur J Nutr

Piglets



Mini-pigs



Barbé et al. 2013, 2014
Food Chem

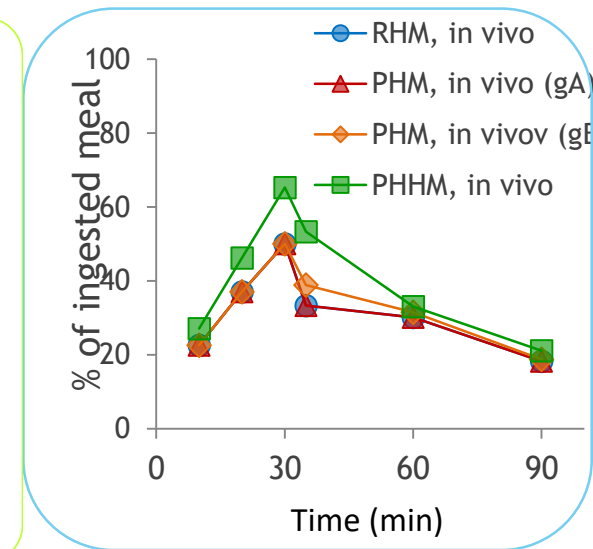
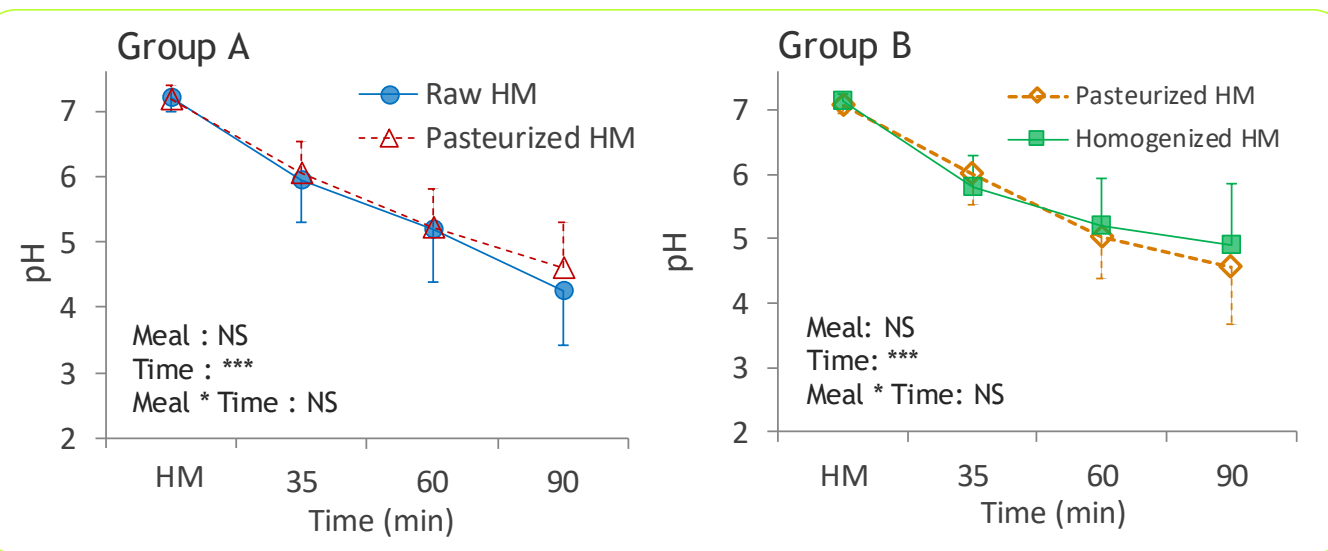
Multi-canulated and
catheterized pigs

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

In vivo (Human) models

Effect of human milk processing on the digestive kinetics of newborns (preterms)

- Holder pasteurization (62.5°C/30min)
- Ultrasonic homogenization



De Oliveira, Am J Clin Nutr; 2016

Sum up of the models available at STLO for simulating digestion

Menard et al. 2018,
Food Chem

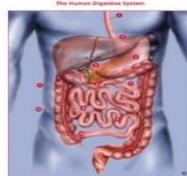


*In vitro static models
(infant, adult)*

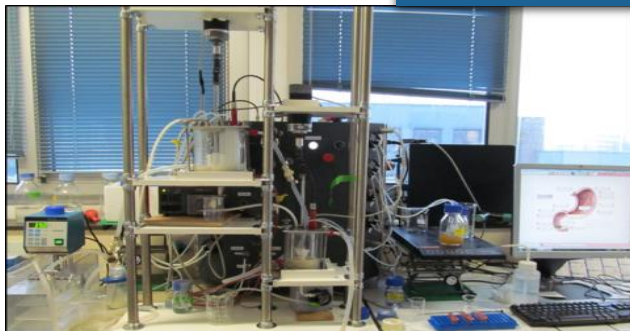
Le Feunteun et al. 2014
Food Bioprocess Tech

*In silico
models*

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



Menard et al. 2014,
Food Chem



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



Human models



Animal models



De Oliveira et al. 2016 Am J
Clin Nutr

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

MERCI



**THANK YOU FOR
YOUR ATTENTION**