Correlation between *in vitro* and *in vivo* data on food digestion. What can we predict with static and dynamic digestion models?

Dr Didier DUPONT

INRA, Rennes, France

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

International Network

Dr. Didier DUPONT, Senior Scientist, INRA, France

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INFOGEST cost

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372 scientists - 140 institutes – 39 countries

Industry involvement

42 private companies are following INFOGEST

Chair
Didier Dupont - France

INFOGEST

Vice-chair
Alan Mackie - UK

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In vitro/in vivo correlations
WG1

Didier Dupont

In vitro semi-dynamic model of digestion
WG2

Alan Mackie

Models for specific populations
WG3

Uri Lesmes

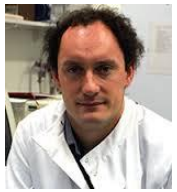
Digestive lipases and lipid digestion
WG4

Myriam Grundy

Frederic Carriere

Digestive amylases and starch digestion
WG5

Nadja Siegert



Fred Warren

In silico models of digestion
WG6

Choi-Hong Lai

Steven Le Feunteun

Guy Vergeres

The "Mind-the-Gap" group

In vitro gastro-intestinal digestion
Consensus INFOGEST protocol

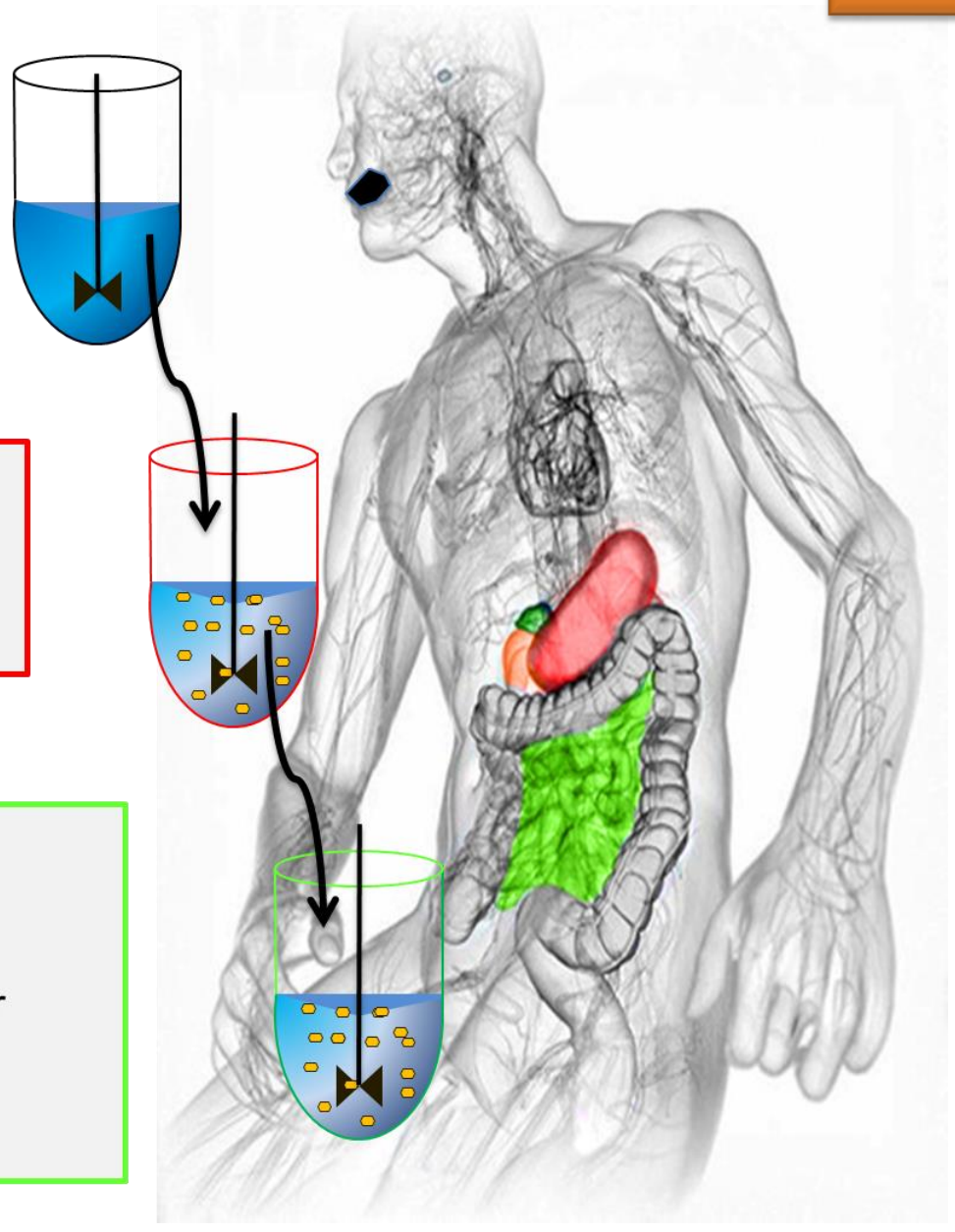
Minekus et al. 2014
Food Funct. 5, 1113-24
Highly Cited Paper (1%)

Oral phase
Mix 1:1 with Simulated Salivary Fluid (SSF)
salivary amylase (75 U/mL)
2 min, pH 7

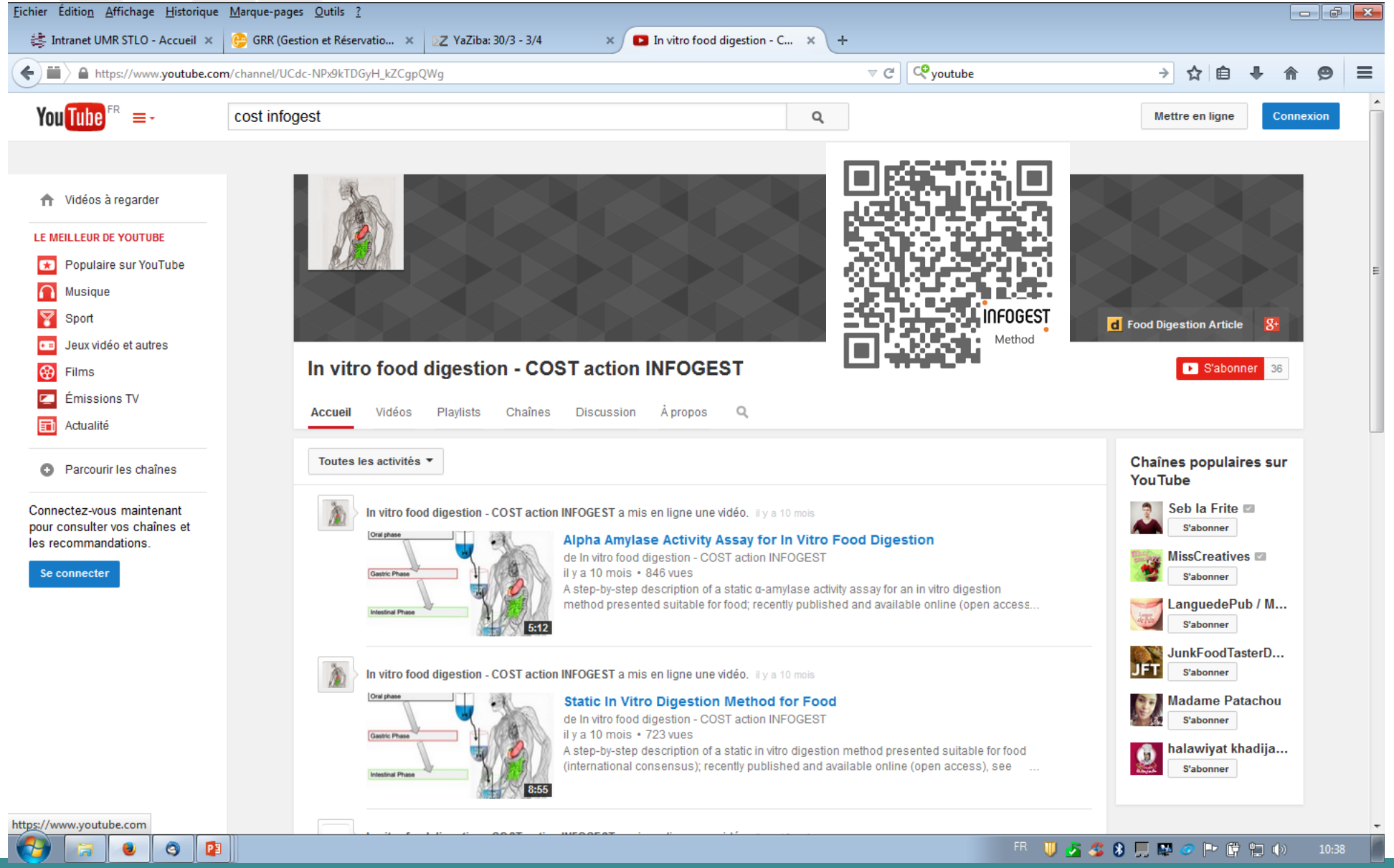
Gastric Phase
Mix 1:1 with Simulated Gastric Fluid (SGF)
Pepsin (2000 U/mL)
2h, pH 3

Intestinal Phase
Mix 1:1 with Simulated Intestinal Fluid (SIF)
Enzymes
- Pancreatin (based on trypsin 100 U/mL) or
- Pure enzymes

Bile (10mM)
2h, pH 7



The consensus model can be learned with videos on YouTube



The International Conference on Food Digestion

The Conference has been created by Infogest and is now an event regularly followed by 200 scientists

INFOGEST
International Conference
Granada, Spain
April 2019

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

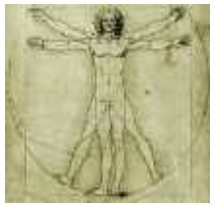
in Granada, Spain, 2-4 April 2019

Static *in vitro* digestion models

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


In vitro

?




In vivo

Main Reasons :

Ethical - Technical – Financial

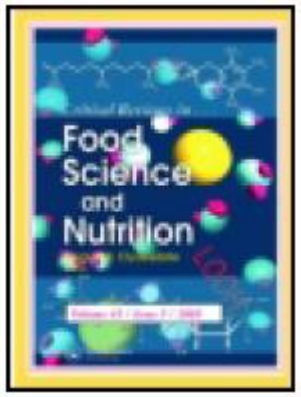
Advantages:

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

Disadvantages:

Impossible to mimic the complexity of the GI tract in a test tube!!!

What can we predict with static digestion models?



CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
https://doi.org/10.1080/10408398.2017.1315362

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REVIEW

Check for updates

Correlation between in vitro and in vivo data on food digestion. What can we predict with static in vitro digestion models?

T. Bohn[a], F. Carriere[b], L. Day[c], A. Deglaire[d], L. Egger[e], D. Freitas[f], M. Golding[g], S. LeFeunteun[f], A. Macierzanka[h], O. Menard[d], B. Miralles[i], A. Moscovici[j], R. Portmann[e], I. Recio[i], D. Rémond[k], V. Santé-Lhoutelier[l], T. J. Wooster[m], U. Lesmes[j], A. R. Mackie[n], and D. Dupont[d]

[a]Luxembourg Institute of Health, Strassen, Luxembourg; [b]CNRS UMR 7282 EIPL, Marseille, France; [c]Agresearch, Palmerston North, New Zealand; [d]INRA UMR 1253 STLO, Rennes, France; [e]Agroscope, Institute for Food Sciences, Bern, Switzerland; [f]INRA UMR GMPA 782, Grignon, France; [g]Massey University, Palmerston North, New Zealand; [h]Gdansk University of Technology, Gdansk, Poland; [i]CIAL CSIC-UAM, Madrid, Spain; [j]Technion—Israel Institute of Technology, Haifa, Israel; [k]INRA UNH UMR 1019, Theix, France; [l]INRA UR 370 QUAPA, Theix, France; [m]Nestlé Research Centre, Nestec S.A., Lausanne, Switzerland; [n]University of Leeds, Leeds, United Kingdom

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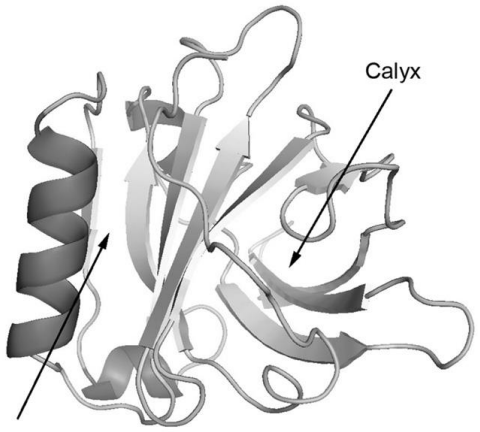


Interaction with PC slows β-lg gastric digestion

* Static *in vitro* digestion models can be useful to compare series of samples or understand molecular mechanisms

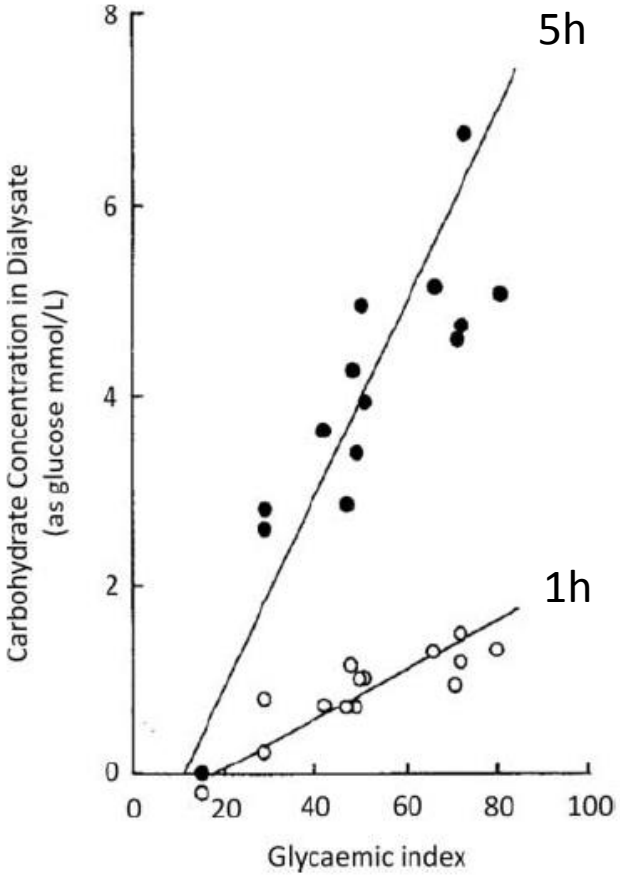
* Static *in vitro* digestion models can be relevant to estimate end-point values such as:
  - Glycaemic index
  - Some micronutrient bioavailability

* Static *in vitro* digestion models are too simple to study more complex phenomena like kinetics of digestion, food structure evolution in the GI tract, bacteria survival…

Carbohydrate digestion

14 foods tested:

Lentils
Soya beans
Marrowfat peas
Kidney beans
Wholemeal bread
Instant mashed potato
White rice
Brown rice
White spaghetti
Wholemeal spaghetti
Sweet potato
Buckwheat
Millet
Porridge oats

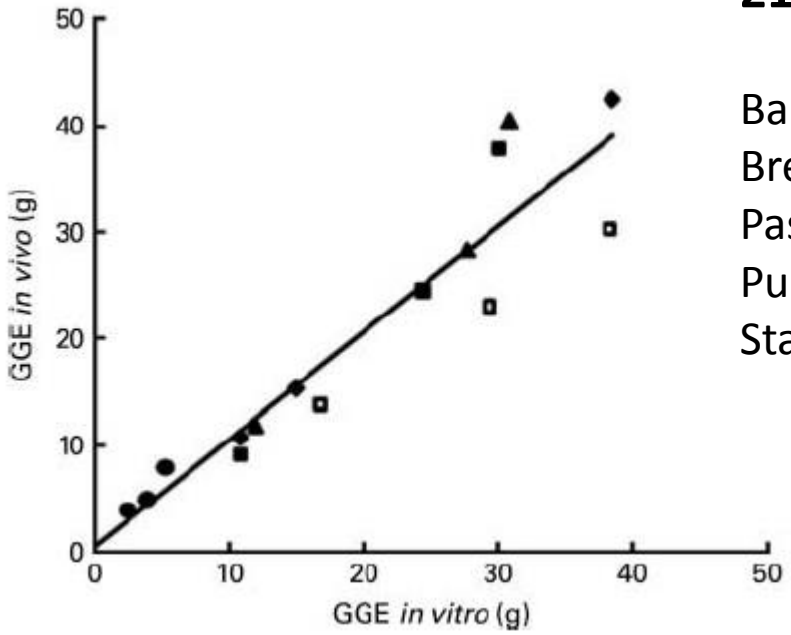


Jenkins et al, 1982. Diabetologia, 22, 450-455

In vitro model requiring fresh human saliva and human post-prandial jejunal juice (no gastric phase)

21 foods tested:

Bakery products
Breakfast cereals
Pasta
Pulses
Starch vegetables

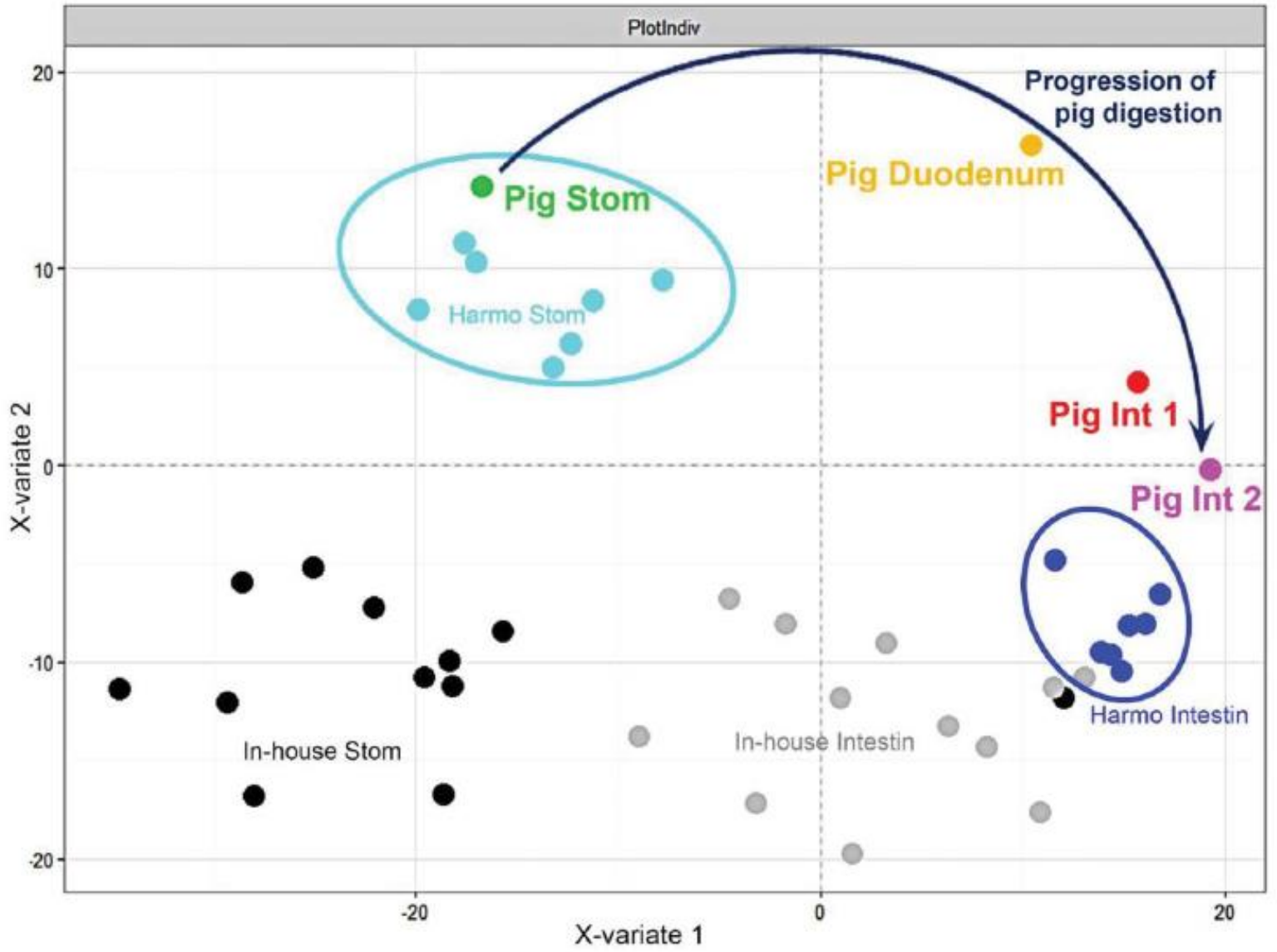


GGE = grams of glucose equivalents

Monro & Mishra, 2010. J Nutr, 140, 1328-1340

Oro-gastrointestinal model with an in vivo oral phase and the combined use of amyloglucosidase and pancreatin

Comparing the peptidome obtained during Skim Milk Protein digestion



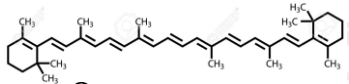
Egger et al. 2018 Food Res Int, submitted

The INFOGEST consensus protocol is relevant for protein digestion

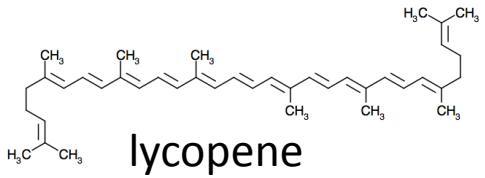
What about for the other nutrients?

Future experiments in WG4 and WG5

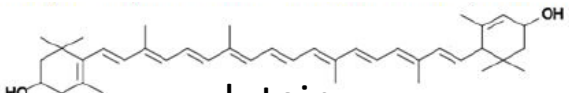
Bioaccessibility/bioavailability of carotenoids



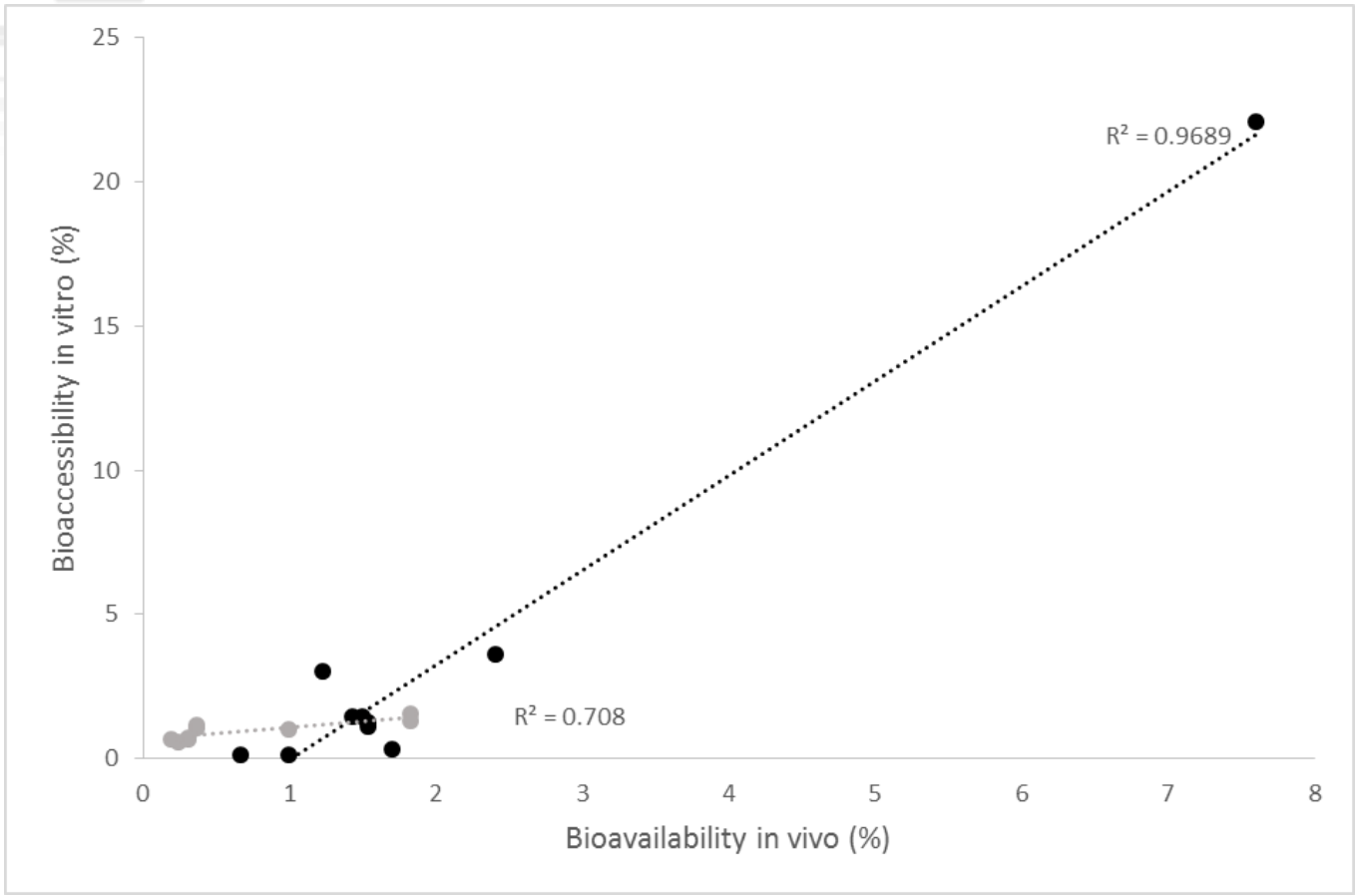
β-carotene



lycopene



lutein



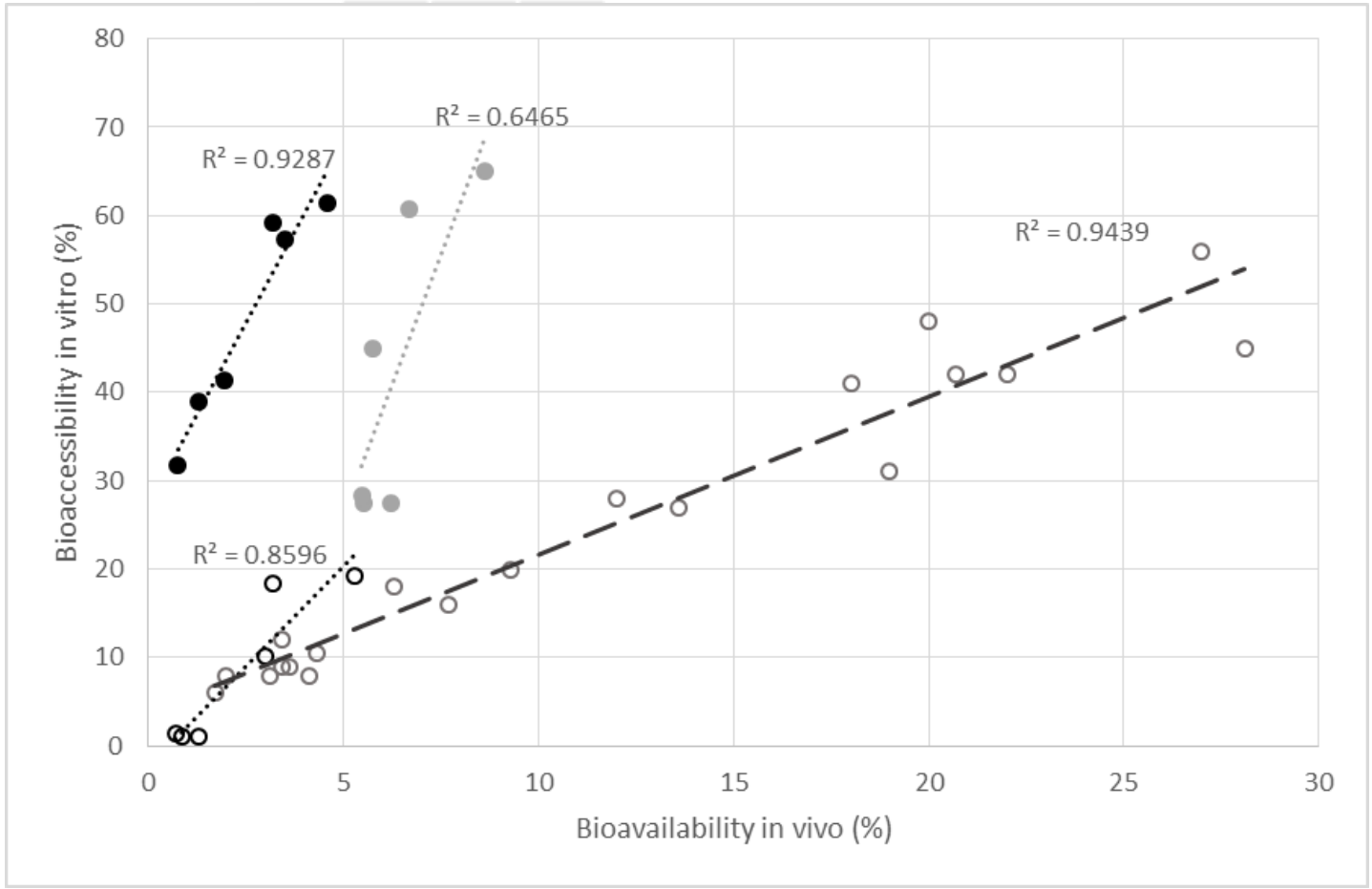
Two-step digestion models + Caco-2

β-carotene ✓

Lycopene ✗

Correlation of bioaccessibility and bioavailability of various carotenoids (lycopene, beta-carotene, lutein), as presented by Reboul, et al. 2006 (black points) and Alminger, et al. 2012 (grey points)

Bioaccessibility/bioavailability of iron



In conclusion, for micronutrients:

Direction of bioavailability (higher, lower, equally well) appears to be generally predictable by in vitro digestion

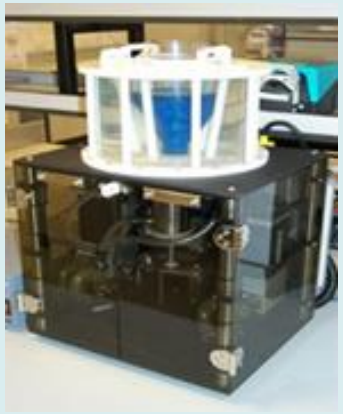
But does mostly not predict the magnitude of bioavailability in humans

Transport, metabolism, colonic changes (especially for polyphenols), biodistribution and (renal) excretion affect bioavailability

Correlation of iron bioaccessibility (dialysis method) following *in vitro* digestion from various iron containing test meals and bioavailability (as estimated via erythrocyte incorporation) employing the same formulations. Empty black dots: Data from Walter et al. (2003). Black dots: Data from Aragon et al. (2012). Grey dots: Data from (Davidsson et al. 2002). Empty grey dots: (Sandberg 2005).

Dynamic *in vitro* digestion models

Dynamic Gastric Model (DGM)



Human Gastric Simulator (HGS)

Artificial Colon (ARCOL)

Mono-compartmental models

Digestion Dynamique Gastro-Intestinale (DIDGI)

INFOGEST

Multi-compartmental models

Engineered Stomach and small INtestinal (ESIN)

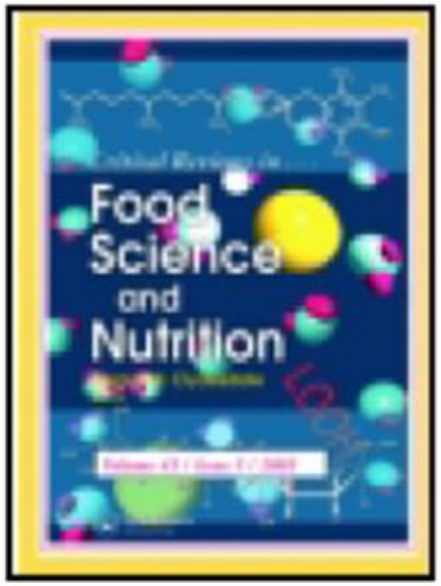
SIMulator of the GastroIntestinal tract (SIMGI)

TNO Gastro-Intestinal ModelTIM

Simulator of the Human Intestinal Microbial Ecosystem (SHIME)

Can dynamic *in vitro* digestion systems mimic the physiological reality?

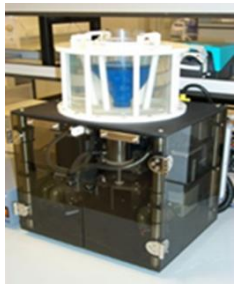
Dupont D.[a*], Alric M.[b], Blanquet S.[b], Bornhorst G.[c], Cueva C.[d], Deglaire A.[a], Denis S.[b], Ferrua M.[e], Havenaar R.[f], Lelieveld J.[f], Mackie A.R.[g], Marzorati M.[h], Menard O.[a], Minekus M.[f], Miralles B.[d], Recio I.[d], Thuenemann E.[i], Van den Abbeele P.[j]



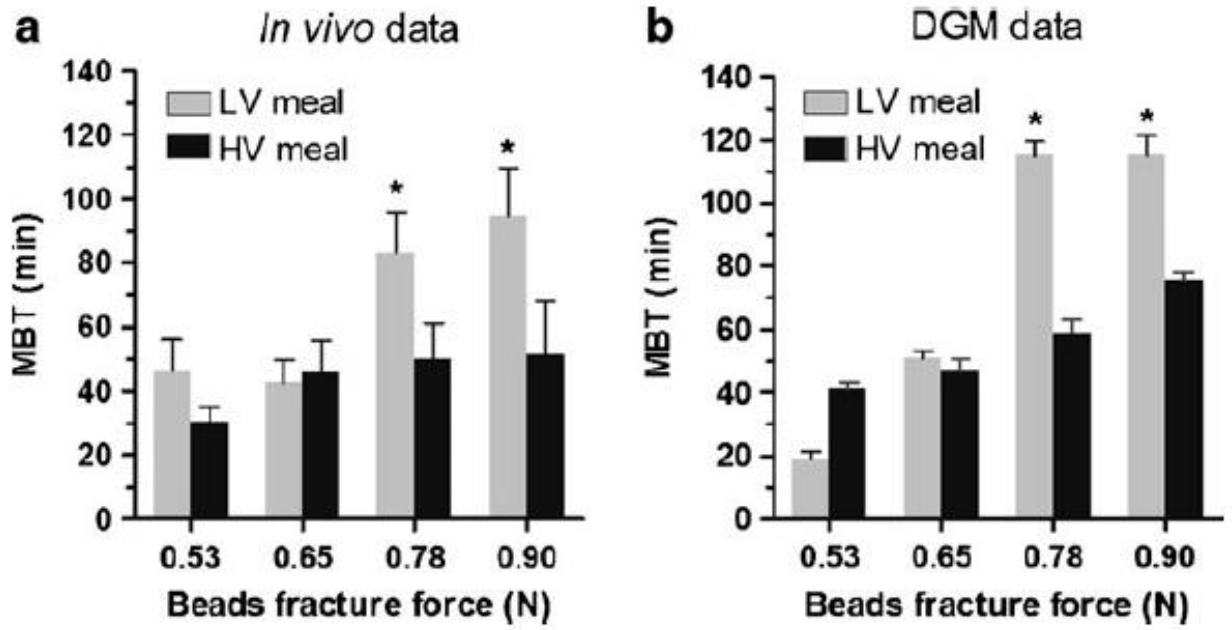
Submitted soon to
Crit Rev Food Sci Nutr

For reprints: didier.dupont@inra.fr

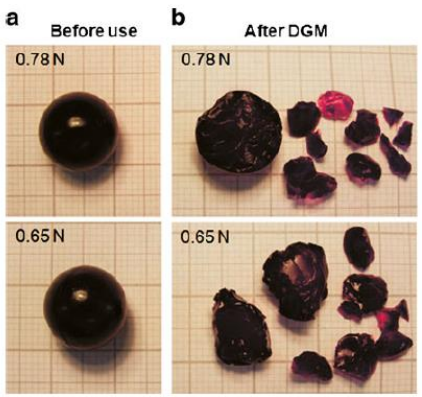
DGM - Simulation of grinding in the stomach

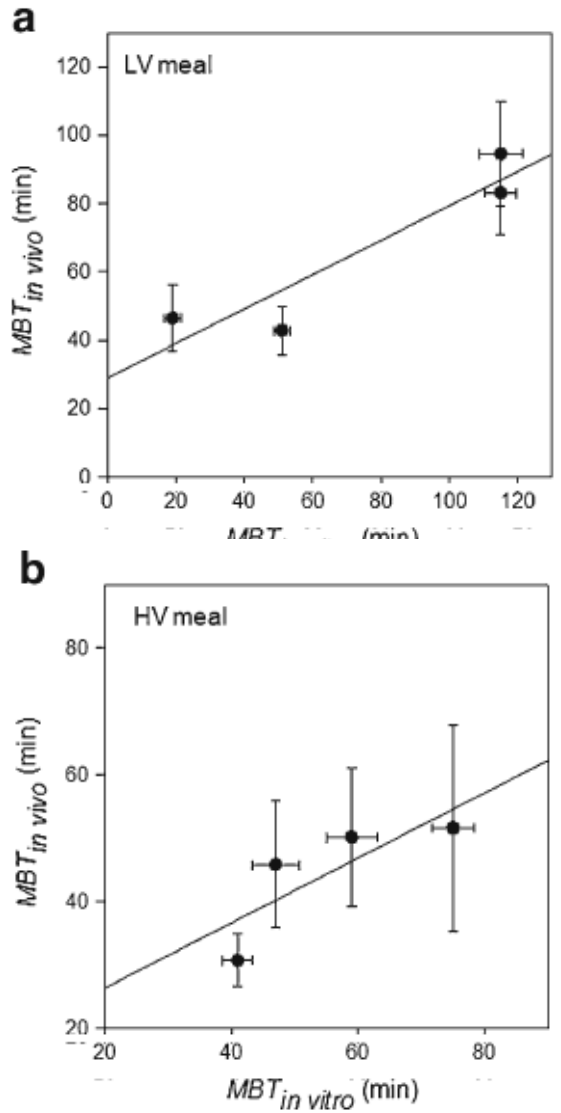


Comparison of the Mean Breaking Time of agar gel beads in low viscosity (LV) and high viscosity (HV) meals

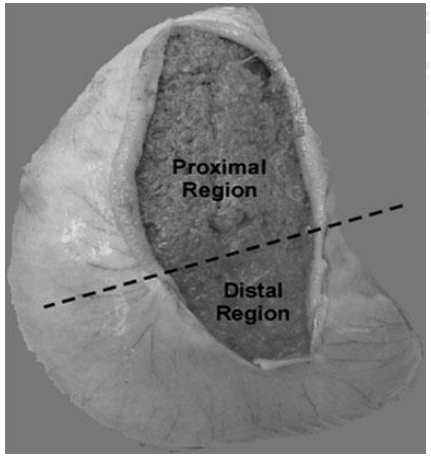


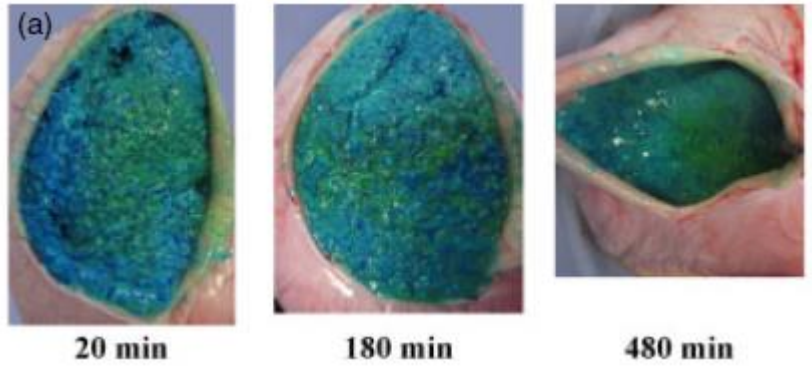
- Increasing the viscosity of the meal reduces the survival time of the harder beads
- Good *in vitro* / *in vivo* correlation

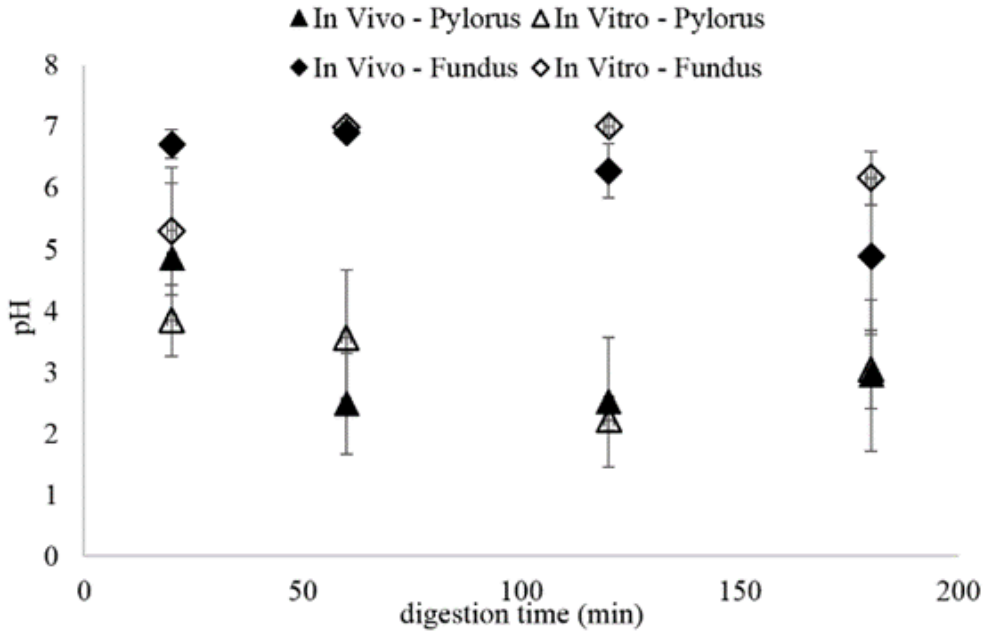


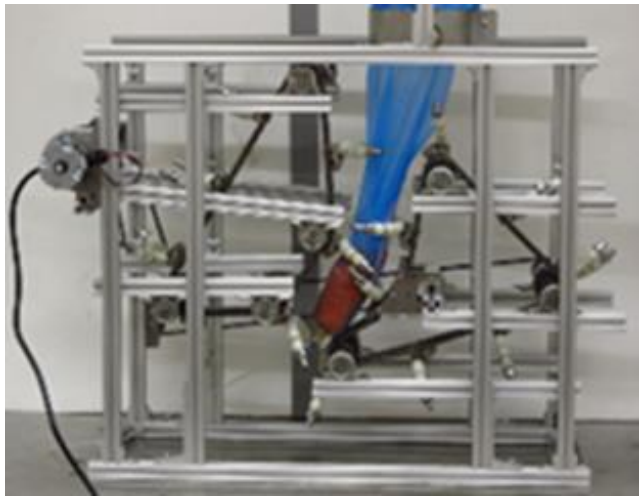


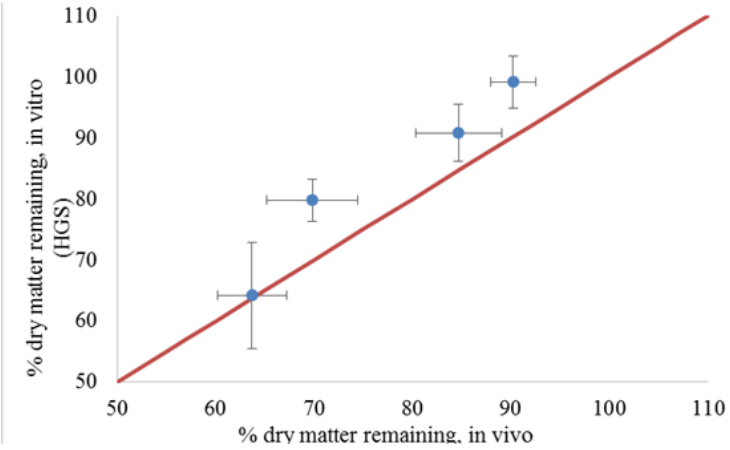
HGS – Comparison of white rice gastric emptying and intragastric pH with growing pigs data

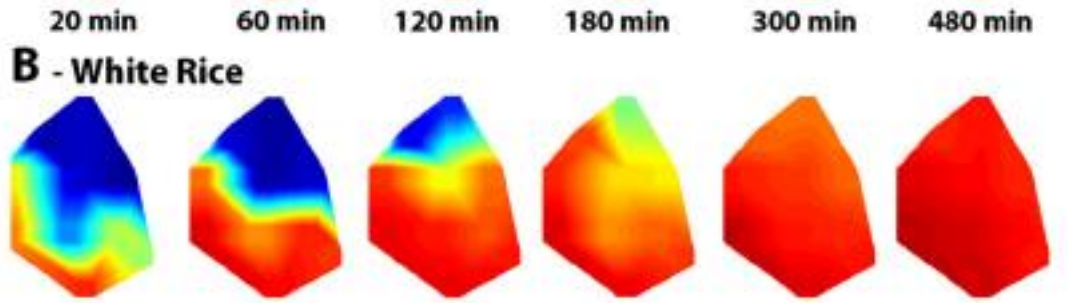




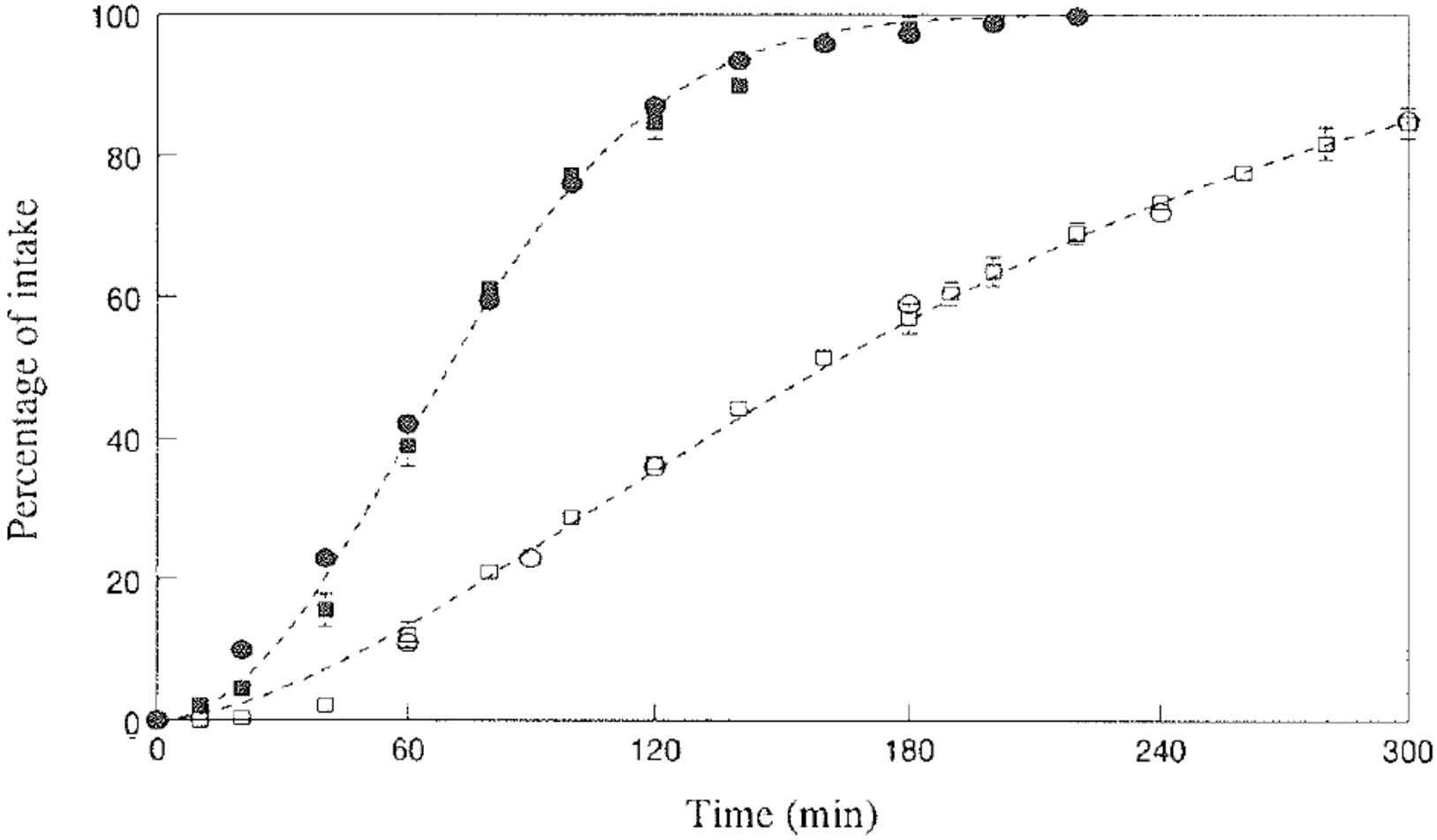






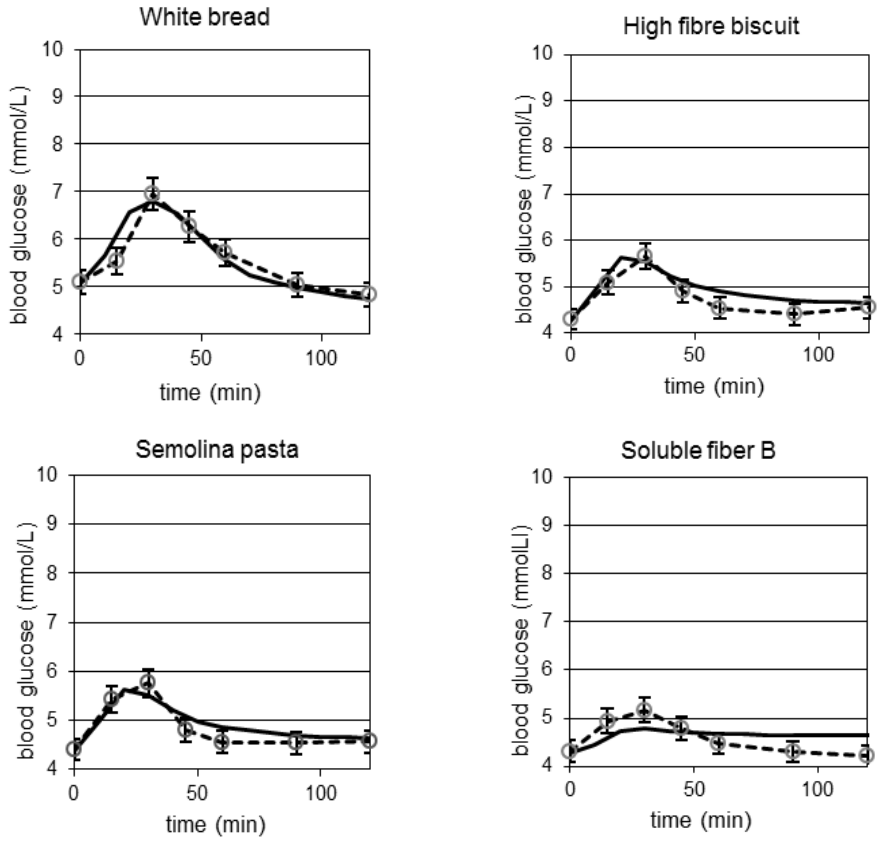


TIM - Transit of dairy products in the gastrointestinal tract

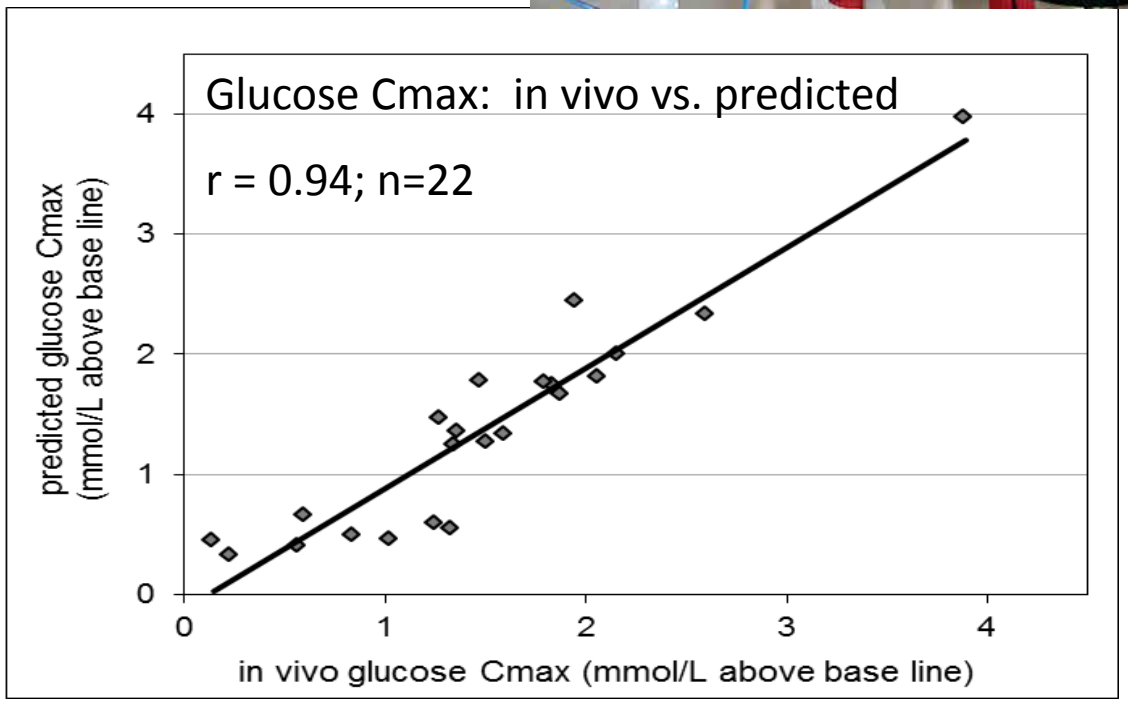


Cumulative gastric and ileal delivery of a meal expressed as a percentage of total intake: *in vivo* (human n=7) gastric (●) and ileal (O) delivery of yoghurt and gastric (■) and ileal (□) delivery of blue dextran in the model simulating the slow transit of yoghurt

TIMcarbo: prediction of human glycemic response curve by combining CHO digestion in tiny-TIM, rapid glucose/fructose analysis and in silico modelling.



Glycemic response: In vivo (dotted) vs. predicted (solid)



Bellmann et al., *submitted for publication*

SHIME® – *in vitro / in vivo production* of Short-Chain Fatty Acid during fermentation of various polysaccharide sources

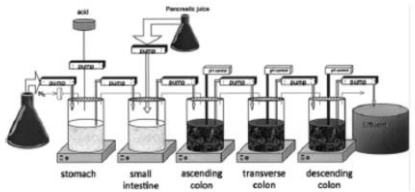
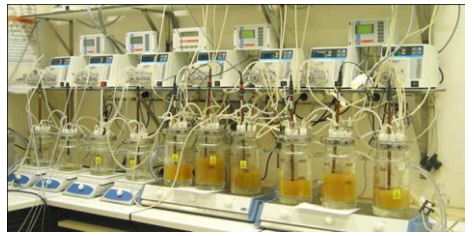
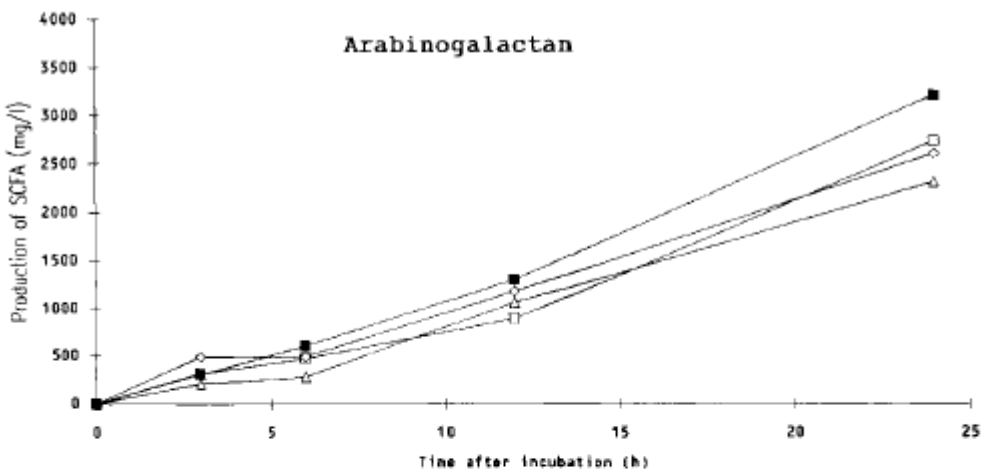
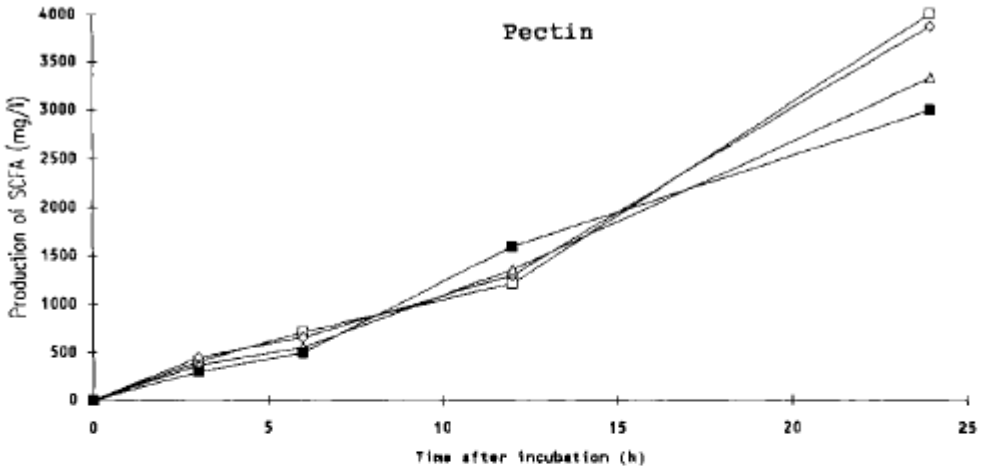
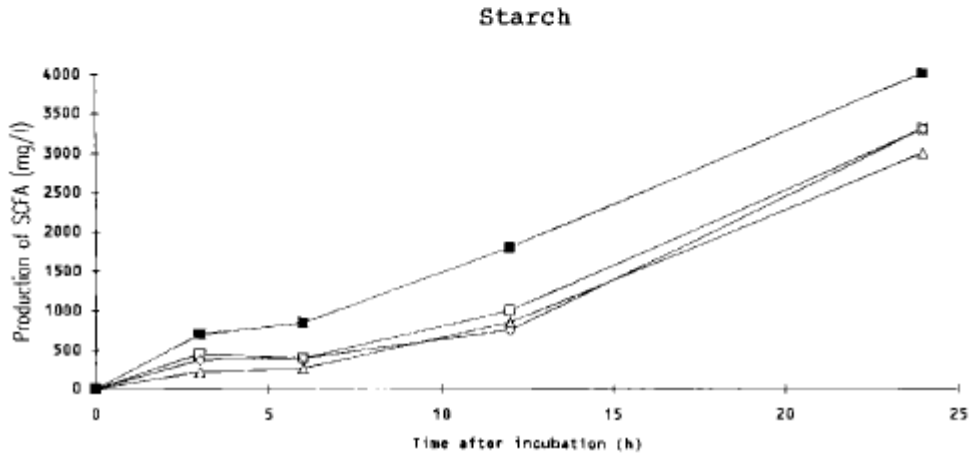


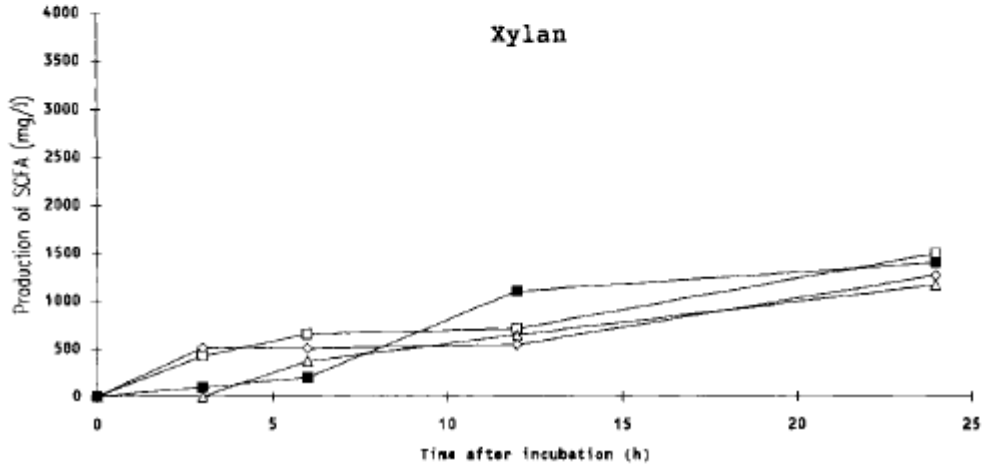
Fig. 27.1 Schematic representation of the SHIME®





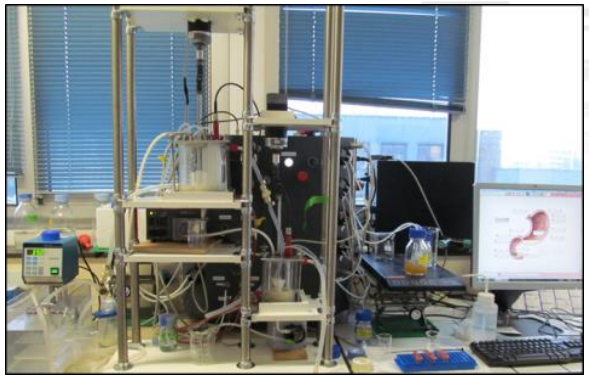






■ In vivo ☐ Ascending colon ◇ Transverse colon △ Descending colon

DIDGI®- Validation of protein digestion in infant formula



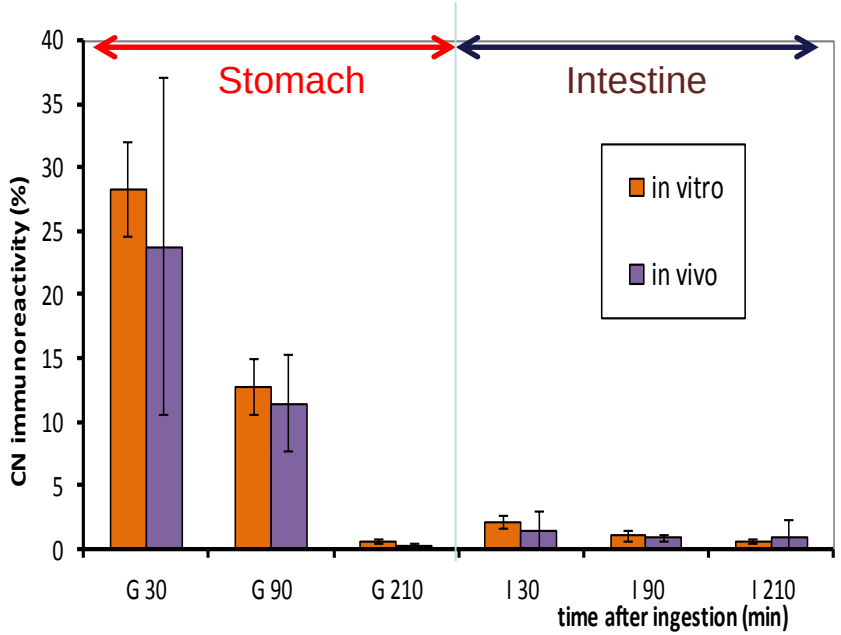
Infant Formula

In vitro

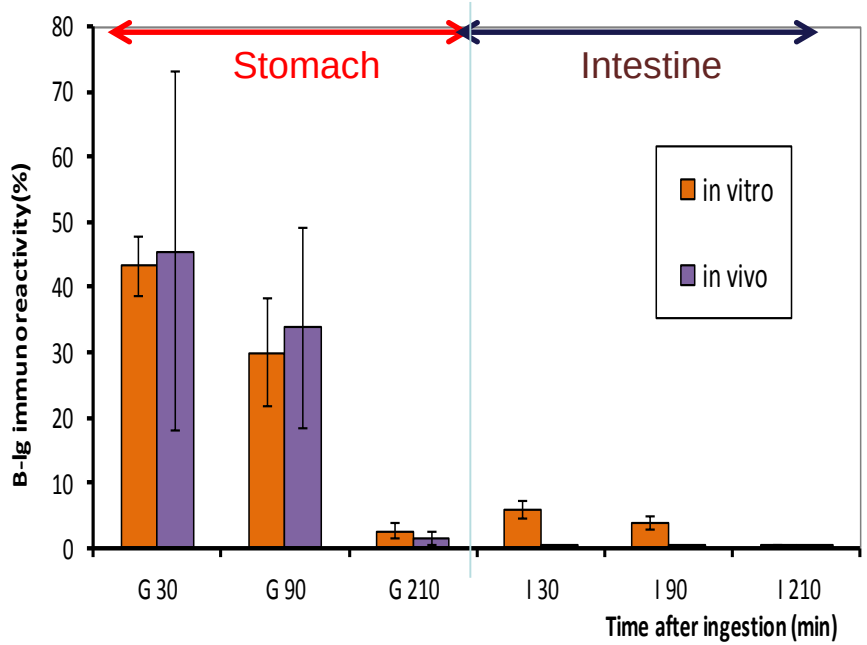
N=3

In vivo

18 piglets



Caseins



β-lactoglobulin

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Menard et al. 2014
Food Chem. 145, 1039-45

INSTITUT CARNOT QUALIMENT

Conclusion

☞ Static *in vitro* digestion models are interesting for comparing large series of samples in the same conditions or understanding interaction between constituants

☞ They could also be valuable for predicting end-point values (glycaemic index, micronutrient bioaccessibility…) but are not relevant for investigating dynamic events

☞ Dynamic *in vitro* digestion models can perfectly mimic the physiological reality when parameters are available in the literature

☞ But when a system has been validated for a specific food, does this means that it is relevant for all kind of foods? Can we define large categories of foods (liquids, gels, solids) and validate them?

☞ More validated *in vitro* dynamic digestion models are needed to simulate the digestion process of specific populations (infant, elderly…)

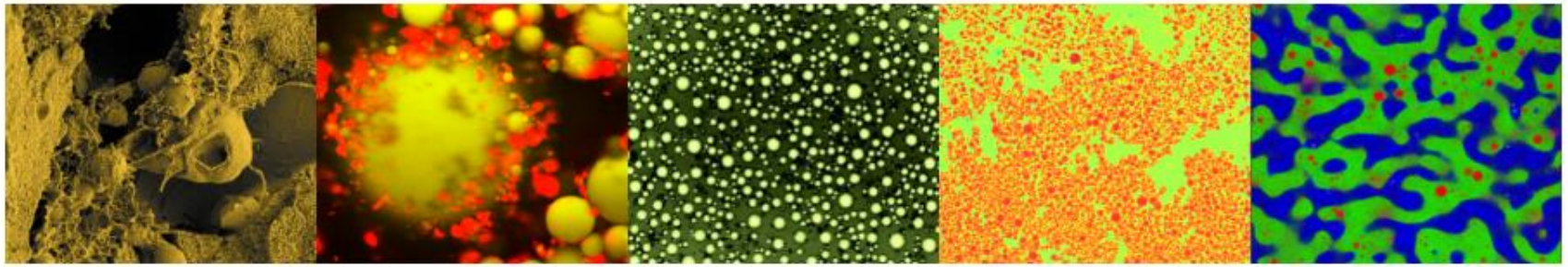
☞ An international consensus could be found on the parametering of *in vitro* dynamic systems

↳ Next objectives of the Infogest network

The next INFOGEST Workshop will be held on the 12-13 of April 2018 in Leeds UK connected to:

17th Food Colloids Conference : Application of Soft Matter Concepts

8th - 11th April 2018
The University of Leeds, UK



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Food Colloids is a biennial conference in the field of physical chemistry of complex foods.

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