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## In vitro amino acid digestibility and availability

Didier Dupont

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2023

INTERNATIONAL SYMPOSIUM  
**DIETARY PROTEIN  
FOR HUMAN HEALTH**

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In cooperation with



# Declaration of Interest

- My primary research focus lies in food digestion, aiming to understand the mechanisms of food breakdown in the different compartment of the gastrointestinal tract and its consequences on human health (infant, adult, elderly)
- I disclose the following [*financial, professional or other*] interest directly relevant to the topic of discussion.

# Declaration of Interest

| Type of interest, <u>and</u> basic descriptive details.                                                                   | Name of company, organization, or institution | Current interest (or year ceased) |
|---------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|-----------------------------------|
| 1. Employment and consulting including service as a technical or other advisor, or other type of management relationship* |                                               |                                   |
| 2. Research support including grants, collaborations, sponsorships, other funding and non-monetary support*               | Sodiaal, Mondelez, Agro-Mousquetaires         | Joint research projects           |
| 3. Financial relationship, including current stock or share ownership or investment interests                             |                                               |                                   |
| 4. Current intellectual property including patents, trademarks, or copyrights (also include pending applications) *       |                                               |                                   |

\*Report evidence within the past 4 years



# In vitro amino acid digestibility and availability

## *Introduction*

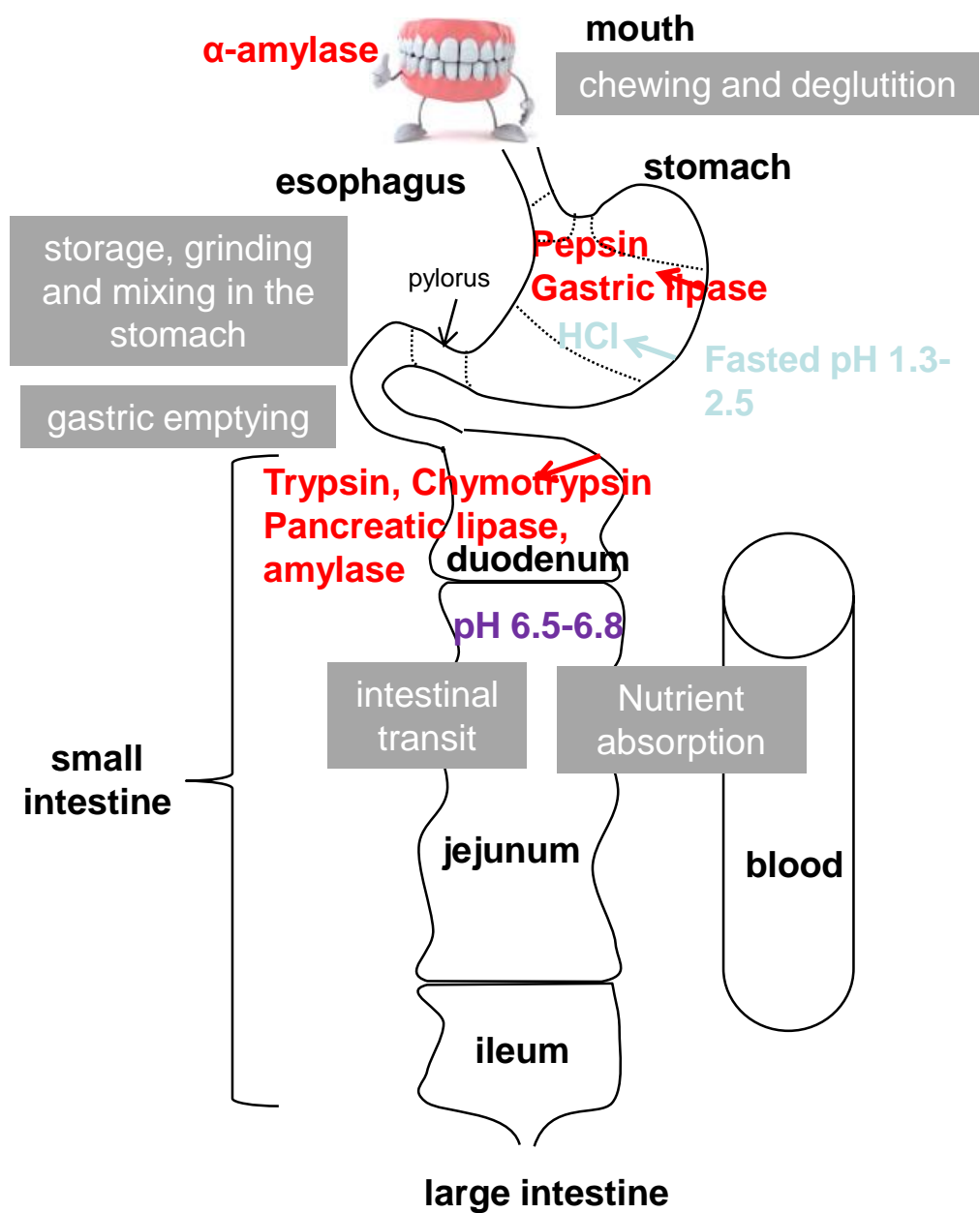


**Didier DUPONT**

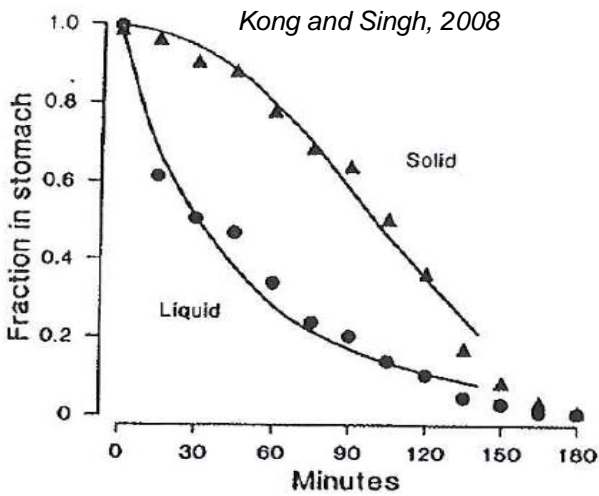
INRAE, Rennes, France



# The digestive process



From Roger Lentle, Massey Univ. NZ



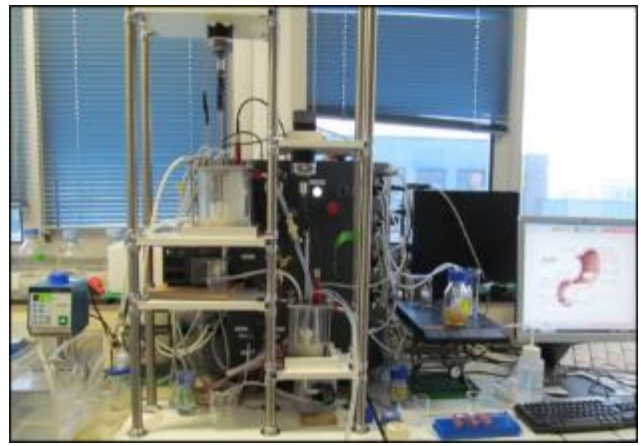
Gastric phase = a very complex but crucial step for the kinetics of the whole digestion process

# Models available to study digestion

**INFOGEST**



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



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



*In silico  
models*

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



*Human  
models*



*Animal models*



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



Consist in a series of bioreactors where the enzymatic and physicochemical conditions of the different compartments of the gut will be mimicked

It is static since the conditions are kept constant throughout the different steps. No flow of the food between the compartments. A step starts when the previous one has been fully completed

Widely used by the scientific community

## Main Reasons :

Ethical - Technical – Financial

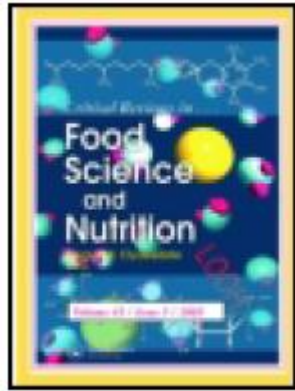
## Advantages:

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!!!







REVIEW

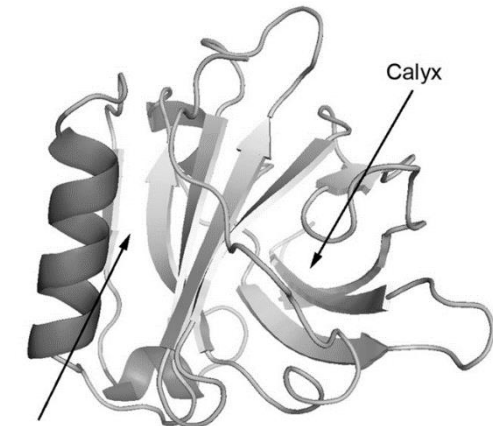


## Correlation between *in vitro* and *in vivo* data on food digestion. What can we predict with static *in vitro* digestion models?

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

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

**CONTACT** Dr. D. Dupont  [didier.dupont@inra.fr](mailto:didier.dupont@inra.fr)  INRA UMR 1253 STLO, 65, rue de St Brieuc, 35042 Rennes Cedex, France.



Putative secondary binding site

Interaction with PC slows  $\beta$ -Ig 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 bioaccessibility
- Protein digestibility

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

**Bohn et al. 2018**  
**Crit Rev Food Sci Nutr**  
**215 citations**  
**Highly Cited**

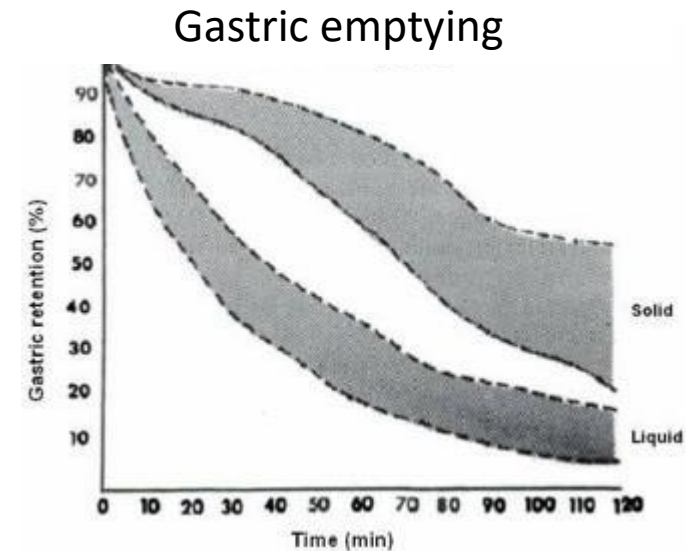
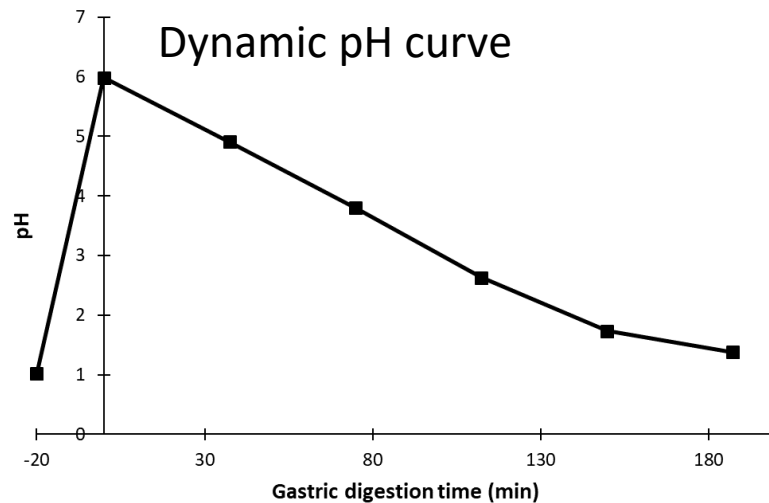
# Semi-dynamic in vitro model

Mulet-Cabero et al. 2020  
Food & Function  
172 citations  
Highly Cited



Simulation of:

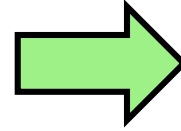
- ✓ Progressive acidification
- ✓ Gradual enzyme and fluids secretion
- ✓ Continuous emptying



# What does it simulate?

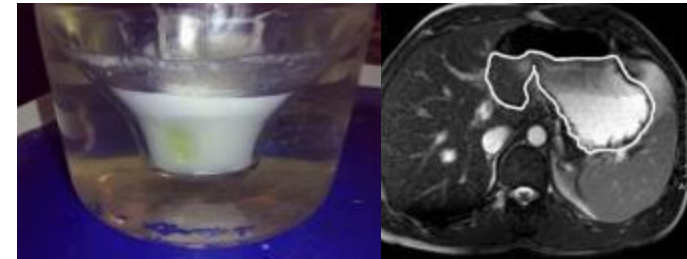
## Simulation of:

- ✓ Progressive acidification
- ✓ Gradual enzyme and fluids secretion
- ✓ Continuous emptying

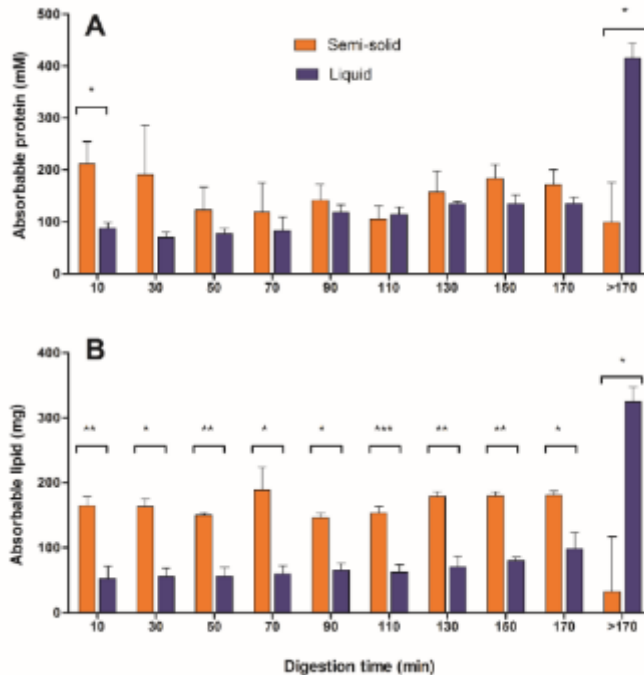
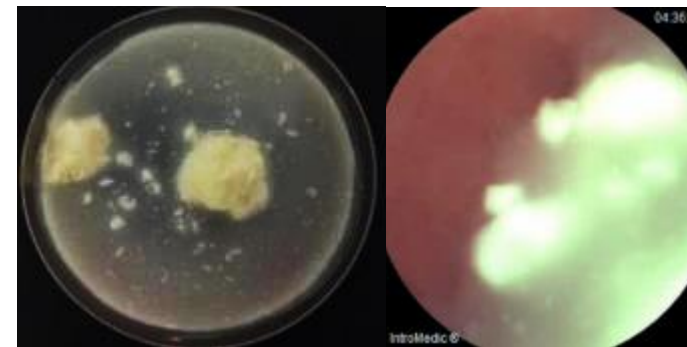


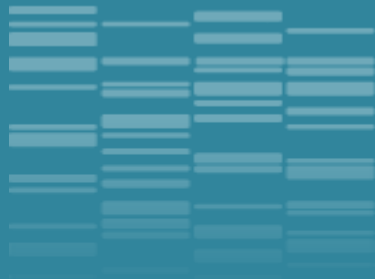
- ✓ Rate of nutrient digestion
- ✓ Structural changes in stomach

## Layering



## Coagulation



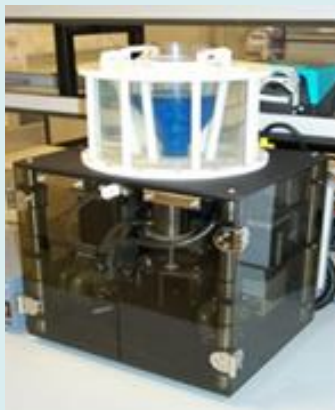


## Dynamic *in vitro* digestion models





Dynamic Gastric Model (DGM)



Human Gastric Simulator (HGS)



Artificial Colon (ARCOL)

### Mono-compartmental models

### Multi-compartmental models



Digestion Dynamique Gastro-Intestinale (DIDGI)



Dupont et al. 2018  
Crit Rev Food Sci Nutr  
167 citations  
Highly Cited

Engineered Stomach and small INtestinal (ESIN)



TNO Gastro-Intestinal ModelTIM

SIMulator of the GastroIntestinal tract (SIMGI)



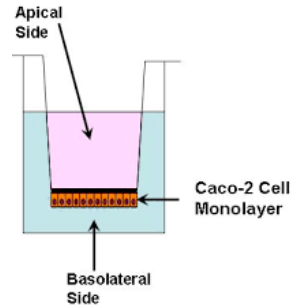
Simulator of the Human Intestinal Microbial Ecosystem (SHIME)



# For bioavailability estimation *in vitro* digestion models must be connected to absorption models

The most oftenly used at the international level:

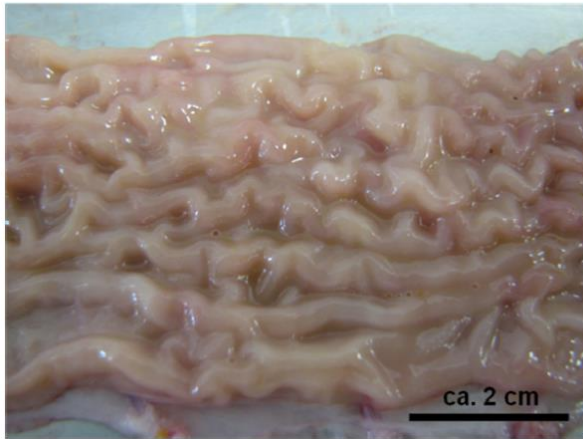
Caco2 cell monolayers



**Kondrashina et al. 2023**  
**Crit Rev Food Sci Nutr**

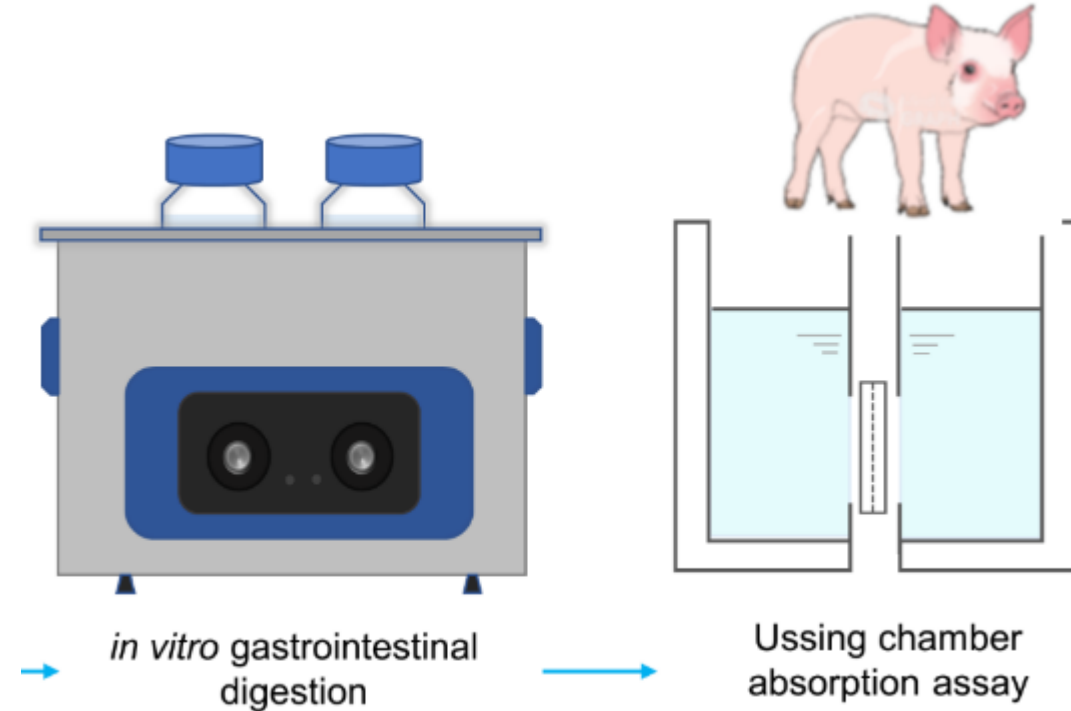
Limit: role of the mucus in absorption?

Porcine Intestinal Mucus



- >95% water
- >5% mucins
- + cholesterol
- + other proteins
- + DNA

More promising: coupling *in vitro* digestion with Ussing chambers experiments?

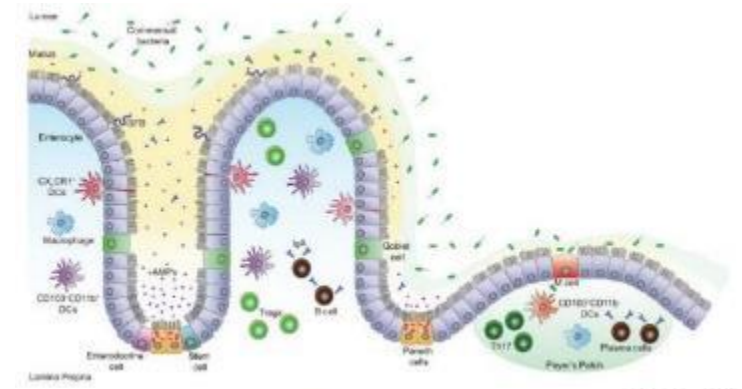


**Ozorio et al. 2021**  
**Foods, 9 (10), 1415**

More complex models: Caco-2 + HT-29-MTX co-cultures  
tri or quadricellular absorption models (with M-cells, immune cells...)

# Colon and intestinal microbiota

Hot topic!!!

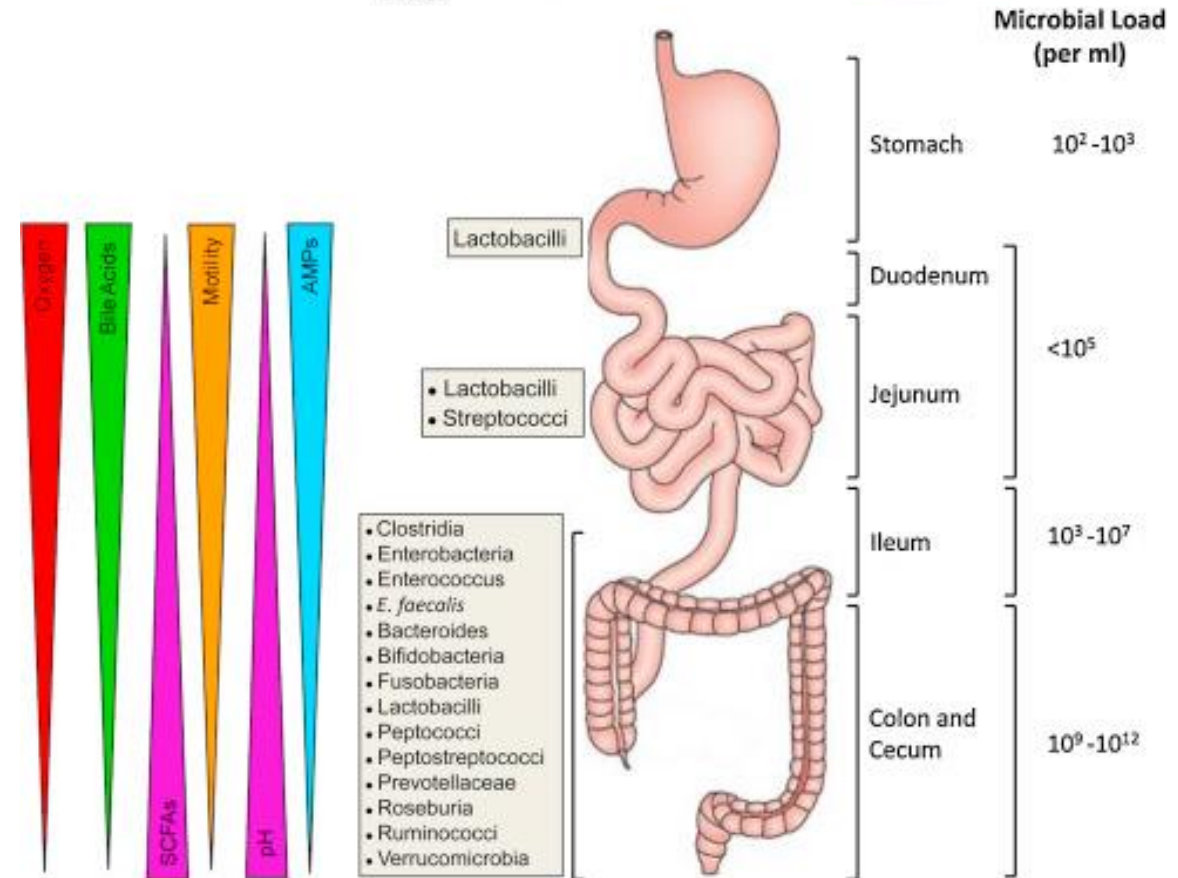


There are bacteria all over the gastrointestinal tract

Most of the scientific studies are focused on the microbiota found in the colon or in the fecal material

Does the microbiota present in the stomach and small intestine play a role in food digestion?

Beside colonic models, most of the in vitro digestion models mimicking the upper part of the gastrointestinal tract lack of the presence of bacteria





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

International Research Network

Dr. Didier DUPONT, Senior Scientist, INRAE, France

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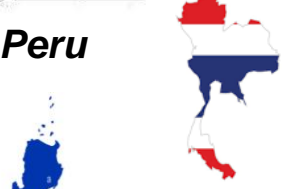
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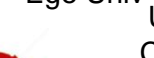


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