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In vitro amino acid digestibility and availability

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2023

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**DIETARY PROTEIN
FOR HUMAN HEALTH**



Food and Agriculture
Organization of the
United Nations



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KŌKIRI - TE HĀ O TE KAI



WAGENINGEN
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IAEA
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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

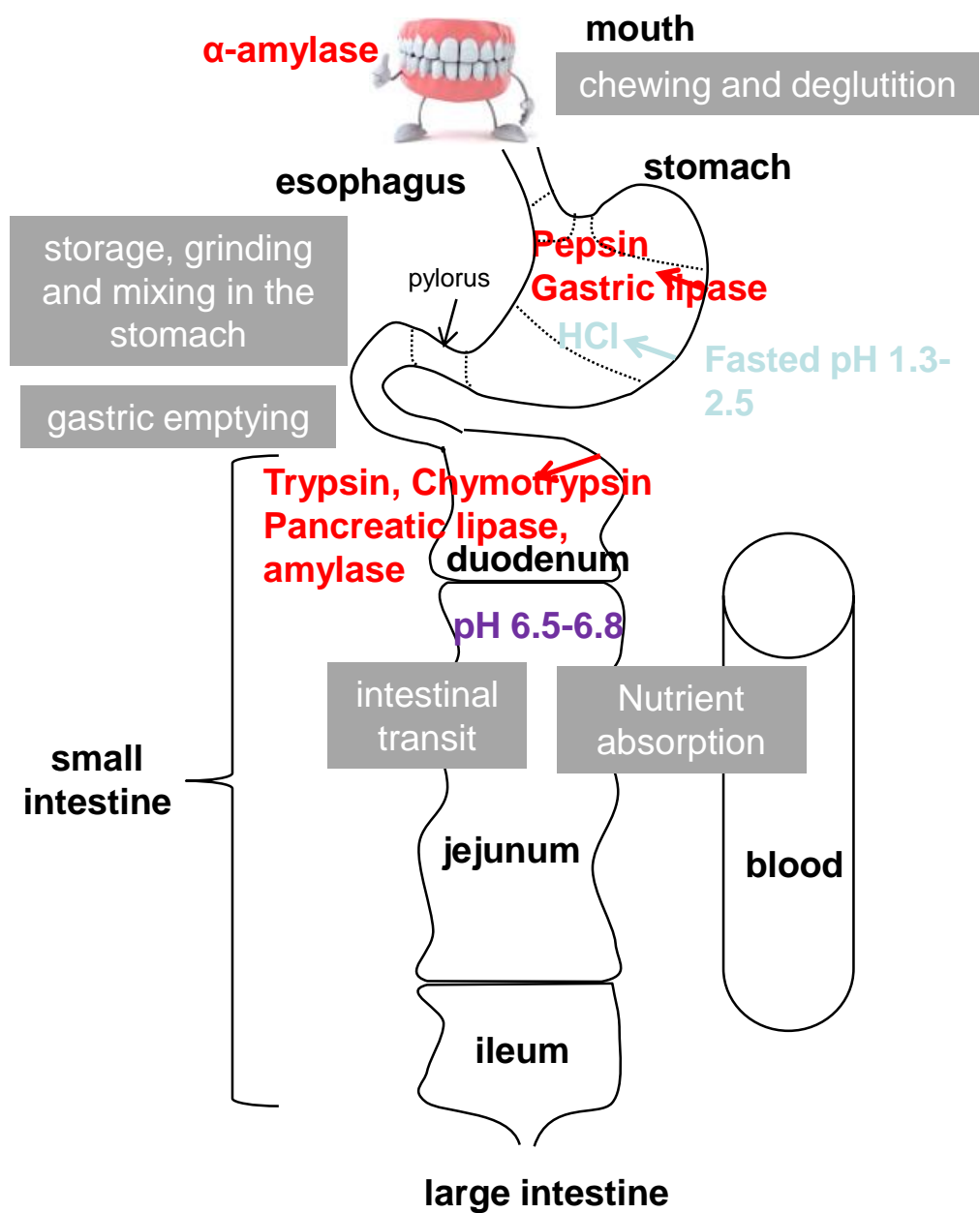


Didier DUPONT

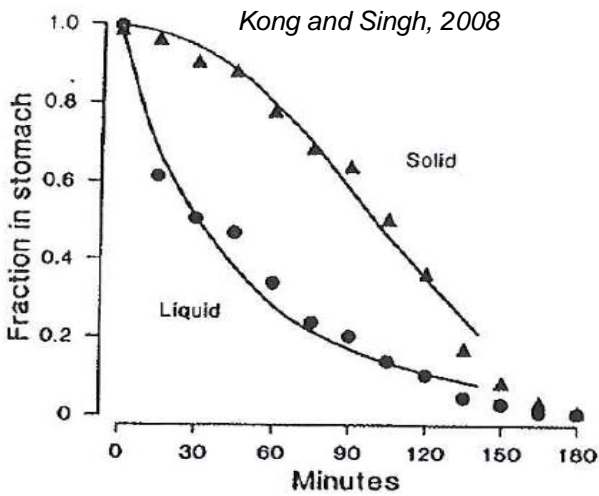
INRAE, Rennes, France



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

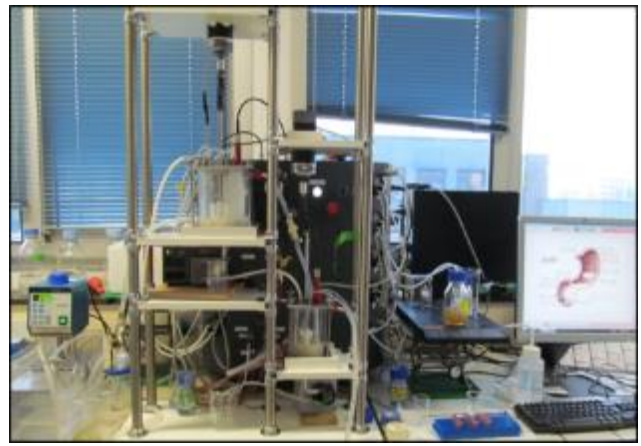
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*In vitro static models
(infant, adult, elderly)*

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

*In silico
models*



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



*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 :

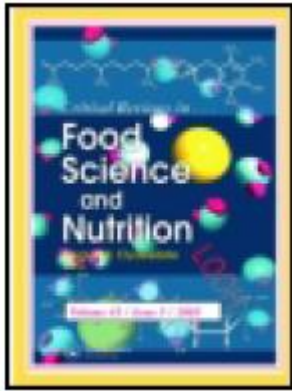
Ethical - Technical – Financial

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

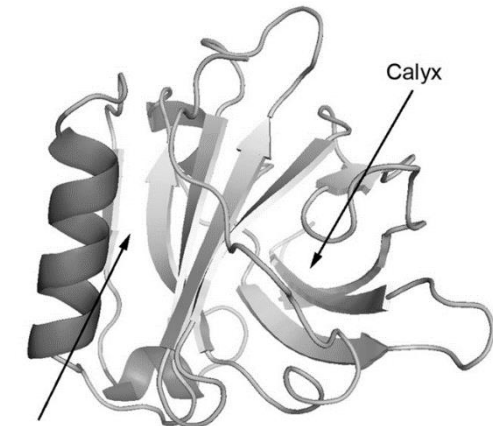


Correlation between *in vitro* and *in vivo* data on food digestion. What can we predict with static *in vitro* digestion models?

T. Bohn^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. Mirallesⁱ, A. Moscovici^j, R. Portmann^e, I. Recio^l, D. Rémond^k, V. Santé-Lhoutellier^l, T. J. Wooster^m, U. Lesmes^j, A. R. Mackieⁿ, and D. Dupont^d

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Putative secondary binding site

Interaction with PC slows β -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

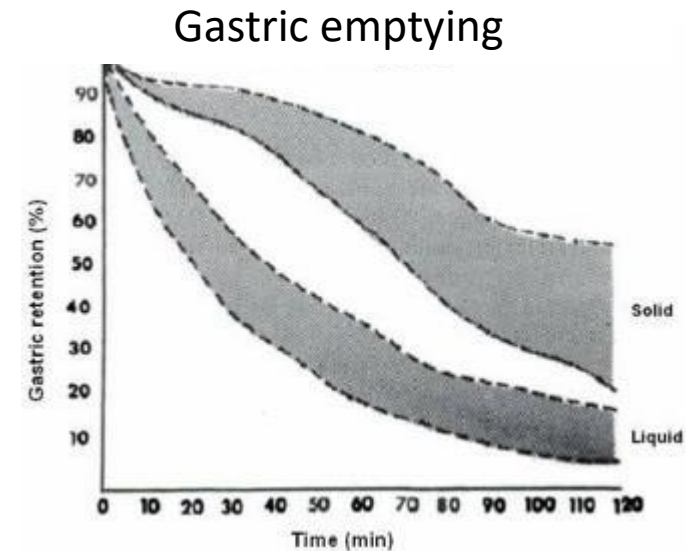
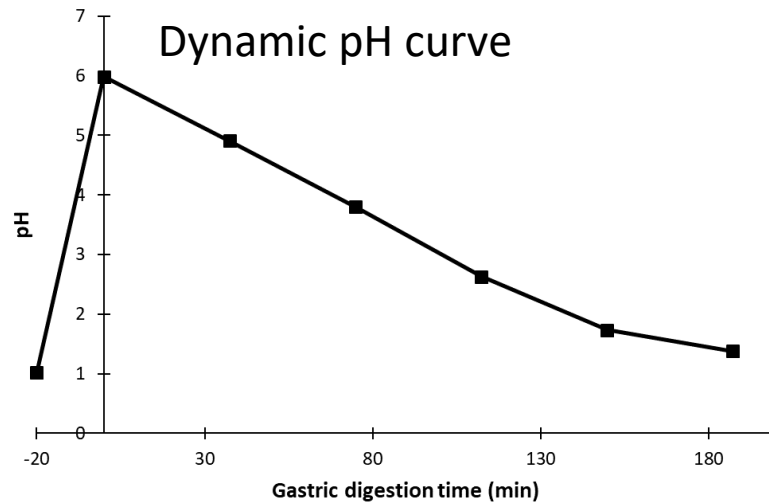
Semi-dynamic in vitro model

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



Simulation of:

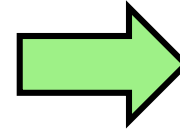
- ✓ Progressive acidification
- ✓ Gradual enzyme and fluids secretion
- ✓ Continuous emptying



What does it simulate?

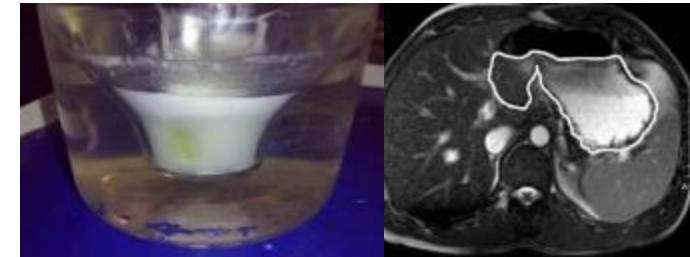
Simulation of:

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

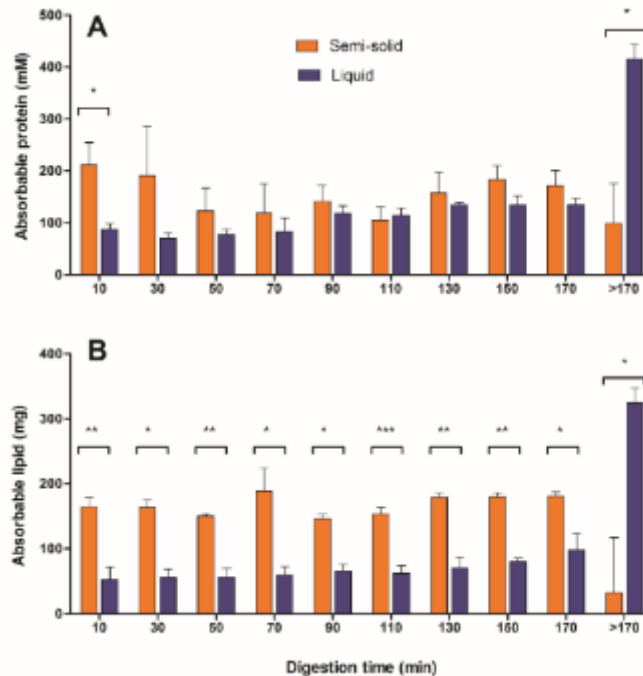
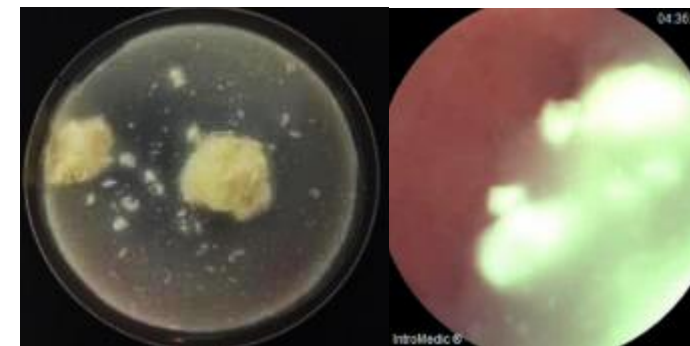


- ✓ Rate of nutrient digestion
- ✓ Structural changes in stomach

Layering



Coagulation

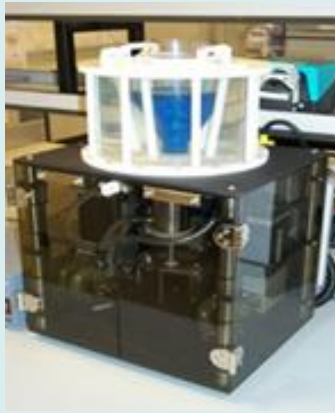




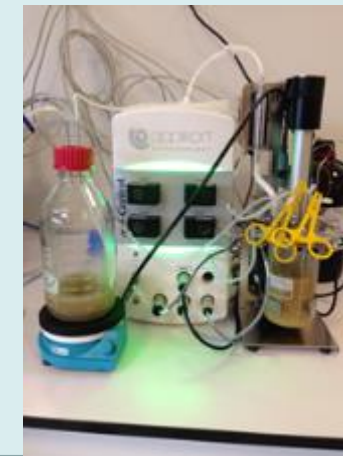
Dynamic *in vitro* digestion models



Dynamic Gastric Model (DGM)

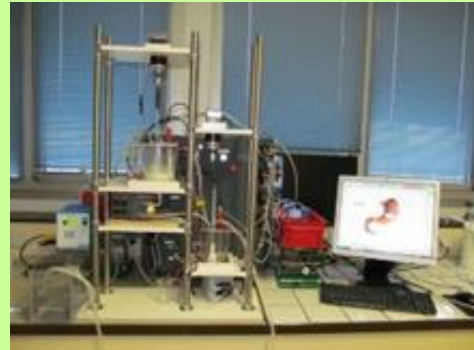


Human Gastric Simulator (HGS)



Artificial Colon (ARCOL)

Mono-compartmental models



Digestion Dynamique Gastro-Intestinale (DIDGI)

Multi-compartmental models



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



Engineered Stomach and small Intestinal (ESIN)

SIMulator of the GastroIntestinal tract (SIMGI)



Simulator of the Human Intestinal Microbial Ecosystem (SHIME)

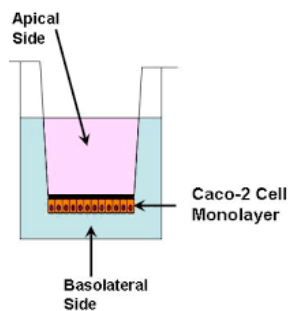


TNO Gastro-Intestinal ModelTIM

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

The most oftenly used at the international level:

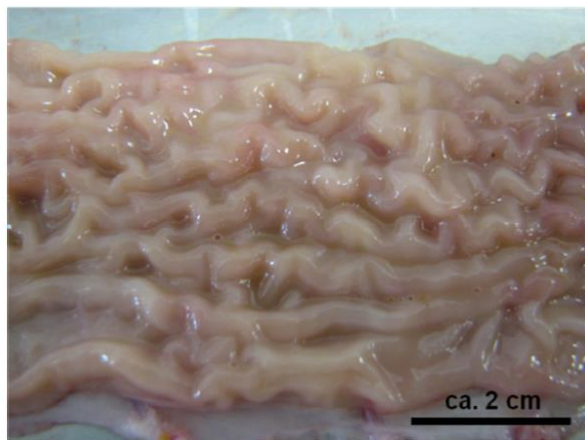
Caco2 cell monolayers



Kondrashina et al. 2023
Crit Rev Food Sci Nutr

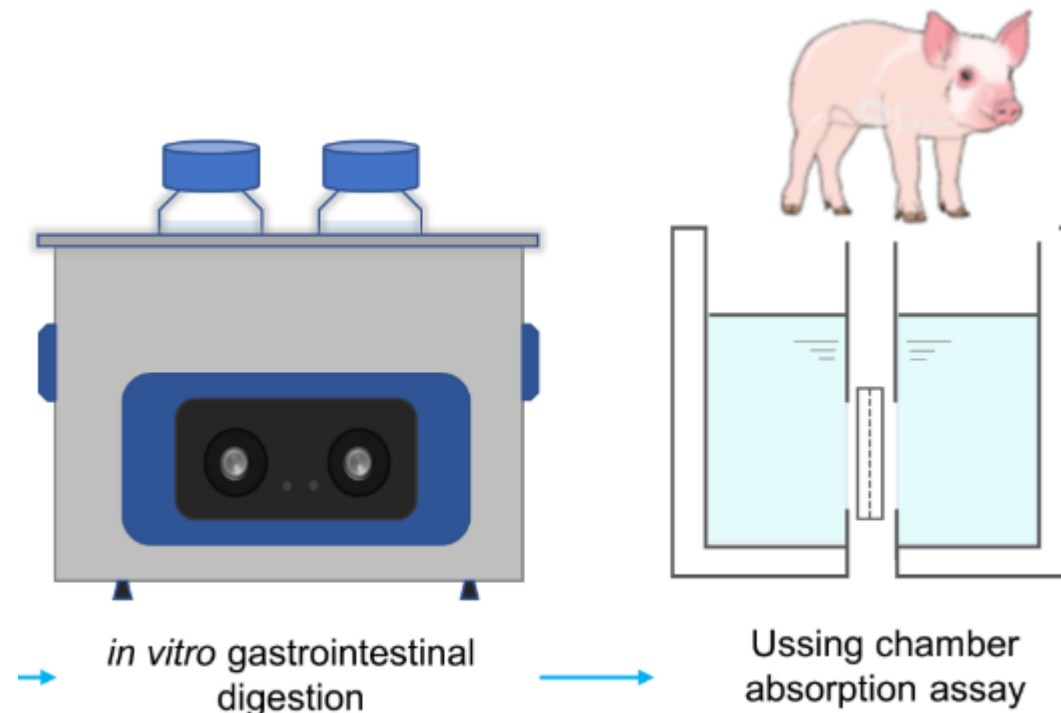
Limit: role of the mucus in absorption?

Porcine Intestinal Mucus



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

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

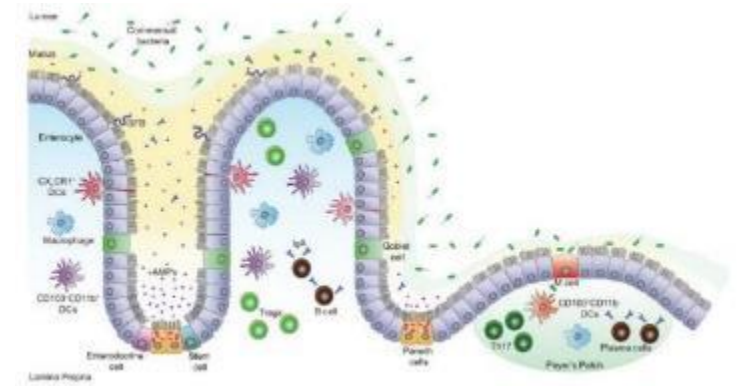


Ozorio et al. 2021
Foods, 9 (10), 1415

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!!!

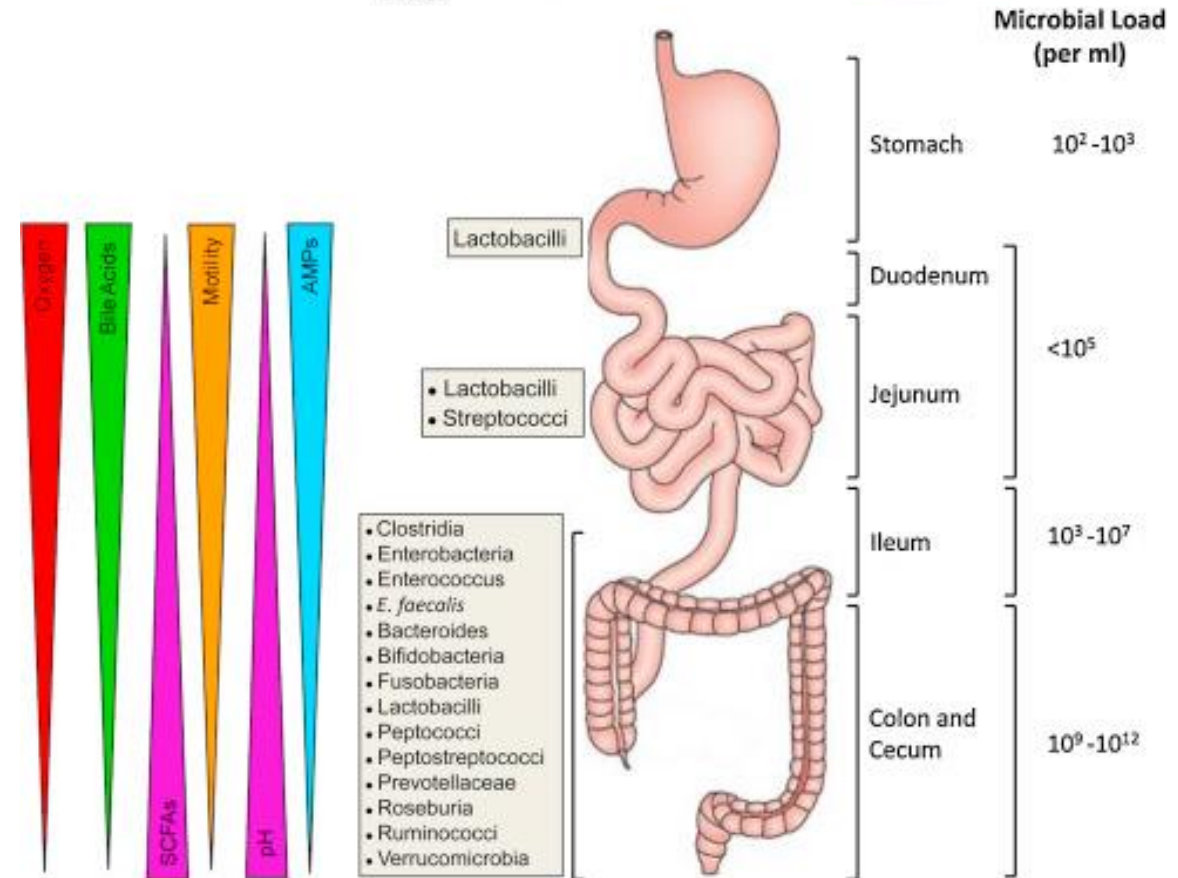


There are bacteria all over the gastrointestinal tract

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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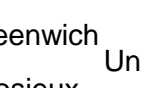
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