



HAL
open science

Structuring food to control its disintegration in the gastrointestinal tract and optimize nutrient bioavailability

Didier Dupont, Steven Le Feunteun, S. Marze, Isabelle Souchon

► To cite this version:

Didier Dupont, Steven Le Feunteun, S. Marze, Isabelle Souchon. Structuring food to control its disintegration in the gastrointestinal tract and optimize nutrient bioavailability. *Innovative Food Science & Emerging Technologies / Innovative Food Science and Emerging Technologies*, 2018, 46, pp.83-90. 10.1016/j.ifset.2017.10.005 . hal-03615663

HAL Id: hal-03615663

<https://hal.inrae.fr/hal-03615663>

Submitted on 21 Mar 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

26 AgroParis Tech INRA
27 Avenue Lucien Brétignières
28 78850 Thiverval-Grignon, France
29 E-mail: steven.le-feunteun@inra.fr

30

31 Dr Sébastien Marze
32 Biopolymers, Interactions, Assemblies
33 Rue de la Géraudière
34 44316 Nantes Cedex 3, France
35 E-mail: sebastien.marze@inra.fr

36

37 Dr Isabelle Souchon
38 Food Process Engineering and Microbiology
39 AgroParis Tech INRA
40 Avenue Lucien Brétignières
41 78850 Thiverval-Grignon, France
42 E-mail: isabelle.souchon@inra.fr

43

44

45 **Abstract**

46 Unravelling the fate of food in the gastrointestinal tract is essential to better understand the health
47 effects of food and fight against diet-related pathologies such as cardiovascular diseases and type-2
48 diabetes, and enable the design of food of high nutritional and sensory qualities to provide humans
49 with a healthy diet. Research to date has mostly considered foods according to their composition.
50 However, the role of the food matrix, i.e. the microstructure-level organization of nutrients and their
51 interactions, in the digestive process was recently demonstrated. This paper summarizes the work
52 done by different groups at the INRA to understand and model food digestion. Integration of the
53 knowledge acquired will serve the development of a reverse engineering approach to design new
54 foods purpose- adapted to meeting the nutritional needs of specific populations like infants or the
55 elderly.

56

57 **Keywords**

58 Food matrix – digestion – health – modeling – reverse engineering – nutrient bioavailability

59

60 **Introduction**

61 The past few decades have seen a dramatic increase in diet-related pathologies worldwide. Obesity
62 and its consequences on the increased prevalence of pathologies such as cardiovascular disease and
63 type-2 diabetes affect around 1.5 billion adults in the world today, and most predictions tend to show
64 that the number will reach 3 billion people by the 2030 horizon (WHO, 2013). Worldwide, the
65 proportion of adults with a body-mass index (BMI) of 25 kg/m² or greater increased between 1980 and
66 2013 from 28.8% to 36.9% in men and from 29.8% to 38.0% in women (Ng, et al., 2014). This rise in
67 obesity prevalence is observed within all age categories, including the elderly, and appears to be higher
68 for women (15.1%) than men (13.9%). The number of people who die every year from obesity has been
69 estimated at 2.8 million. In France, according to the last national epidemiological study, 6.9 million
70 people are considered obese, and the percentage of obese people has climbed from 8.5% in 1997 to
71 15% in 2012 (Roche, 2012). The increase in obesity is mainly due to (1) consumption of high-calorie
72 foods and (2) a lack of physical activity due to sedentary work patterns, increasing use of mechanized
73 transport, and urbanization. Despite many public information campaigns, it remains difficult to get
74 overweight people to increase their physical activity. The only solution is therefore to offer consumers
75 a wide variety of foods that are less caloric but have similar nutritional, satiation, satiety and sensory
76 properties.

77

78 **The digestive process, or how to transform food into nutrients available for humans**

79 Food disintegration during digestion results in the release of nutrients that will be available to maintain
80 homeostasis. The oral phase is crucial, especially for solid and semi-solid foods. Mastication, the first
81 mechanical step of digestion, transforms food into smaller particles ready to be lubricated. Saliva
82 aggregates masticated food into a bolus before swallowing, and protects the soft mucosal surface from
83 damage by coarse foods. It also acts as a solvent of flavor compounds and contains enzymatic activities
84 that initiate macronutrient digestion, particularly hydrolysis of carbohydrates. Salivary α -amylase can
85 hydrolyze a large proportion of starch before food reaches the small intestine (Bornhorst & Singh,
86 2012) depending on the food buffering capacity able to maintain gastric pH within a range where this
87 enzyme is still active and on the dramatic loss of structural organization of starch granules
88 (gelatinization) in response to heat treatment. The oral phase also allows the release of molecules
89 responsible for the flavor that can act as biological signals and generate satiety. When food enters the
90 stomach, the bolus will encounter a dramatically different set of physical-chemical conditions to the
91 oral cavity. Acid secretions produced by the gastric mucosa and digestive enzymes such as gastric lipase
92 or pepsin will transform the bolus into a chyme, dramatically affect food structure, and modulate

93 gastric emptying rate. Gastric emptying rate depends on the caloric charge of the meal and the
94 osmolarity and structures of the chyme. Macronutrient hydrolysis, initiated in the stomach for proteins
95 and lipids and in the mouth for carbohydrates, will be completed in the small intestine under the action
96 of highly efficient enzymes such as pancreatic lipase, trypsin, chymotrypsin, elastase and pancreatic α -
97 amylase. This is also where most nutrient absorption will take place, due to the structure of the
98 intestinal epithelium which is covered with villi that increase the absorption surface. The intestinal
99 epithelium also releases myriad enzymes that help complete the breakdown of nutrients before their
100 absorption (Babusiak, Man, Petrak, & Vyoral, 2007). The epithelium is also covered by a mucus layer
101 whose protective effect against pathogenic bacteria stems from the presence of glycoproteins, i.e. the
102 mucins, but also DNA granules generated by epithelial cell apoptosis. Bile salts facilitate the ability of
103 a food particle to pass this protective layer (Macierzanka, Mackie, Bajka, Rigby, Nau, & Dupont, 2014).
104 Finally, undigested constituents, in particular both soluble (pectin, alginate, carrageenans, etc.) and
105 insoluble (cellulose, hemicellulose, lignin) dietary fiber, will reach the large intestine where they will
106 be metabolized by the intestinal microbiota. The whole digestive process is regulated by
107 gastrointestinal hormones that can slow down or accelerate gut motility. For instance, an excess of
108 triglycerides reaching the ileum (distal part of the small intestine) will end up in the production of GLP1
109 and PYY peptides that will slow down gastric emptying, allowing better hydrolysis and absorption of
110 lipids. Sensors are visibly found along the entire gastrointestinal tract (and especially in the duodenum)
111 where they are able to bind dietary peptides, free fatty acids and micronutrients to regulate the
112 digestive process (Akiba & Kaunitz, 2014). The importance of nutrient homeostasis for human health
113 is manifest, yet little is known about direct nutrient-sensing mechanisms. This is currently a hot
114 research topic, and lipid, amino acid and glucose sensing mechanisms and signaling events were
115 recently reviewed (Efeyan, Comb, & Sabatini, 2015).

116

117 **Why do we need to understand the mechanisms of food disintegration in the gastrointestinal**
118 **tract?**

119 The digestive process has been extensively studied and the events occurring in the gut are relatively
120 well-known, even if nutrient sensing and brain-gut axis connections need further exploration (Efeyan,
121 et al., 2015; Gonzalez-Arancibia, et al., 2016). However, for food itself, less is known about the
122 structural modifications that occur within the gastrointestinal tract. Most studies to date have been
123 limited to either monitoring nutrients in the bloodstream or demonstrating the physiological effects
124 of a diet, with no real understanding of the food disintegration mechanisms involved. A better
125 understanding of the mechanisms underpinning digestion is likely to improve our knowledge on the

126 kinetics of macronutrient hydrolysis and bioaccessibility and, consequently, nutrient bioavailability.
127 This insight should enable the whole digestive process to be mathematically modeled. The main
128 outcome of this kind of mathematical model would be the ability to develop a reverse engineering
129 approach (**Figure 1**) consisting in starting from the biological or nutritional effect we want to obtain
130 and deducing the most appropriate food structure, and consequently the most relevant processing
131 conditions, to obtain it.

132

133 **Does the food matrix structure play a key role in food digestion?**

134 Until recently, it was considered that the structure of the food matrix had a limited impact on food
135 digestion and that the only parameter affecting digestion was food composition in terms of proteins,
136 lipids and carbohydrates. However, in the past few years, new evidences have clearly demonstrated
137 that food matrix structure plays a key role in the kinetics of macronutrient transit and hydrolysis
138 (Parada & Aguilera, 2007; Turgeon & Rioux, 2011). Among the most striking examples, the impact of
139 cooking carrot on carotene bioavailability has been investigated in several *in vivo* studies (Livny, et al.,
140 2003; Tydeman, et al., 2010). At identical composition, carotene release in the gastrointestinal tract is
141 linked to the disintegration of cellular structures, and carotenoid bioaccessibility has been shown to
142 be inversely correlated to carotenoid bioencapsulation. From a processing standpoint, thermal or
143 mechanical processing of fruit- and vegetable-based food products prior to consumption is essential
144 to open up the structural organization in which the carotenoids are embedded and thus enhance their
145 release from the food matrices (Lemmens, Colle, Van Buggenhout, Palmero, Van Loey, & Hendrickx,
146 2014). Another example is the impact of the lipid droplet size of an emulsion on lipid digestion and
147 absorption. Changing the homogenization conditions made it possible to modulate mean lipid droplet
148 size (0.7/10 μm). Consequently, 20–37% of triglycerides were hydrolyzed in the stomach with a 0.7 μm
149 droplet size vs. 7–16% with a 10 μm droplet size (Armand, et al., 1999). Substantial differences were
150 also found in the duodenum, with 57–73% of triglycerides hydrolyzed for the fine emulsion compared
151 to only 37–46% for the coarse one. When the same triglycerides were given to humans in emulsified
152 vs. non-emulsified form as part of a standardized breakfast, the kinetics of postprandial plasma
153 triglycerides was faster and higher for the emulsified form, especially in obese subjects (Vors, et al.,
154 2013). Food structure also has a well-known influence on carbohydrate digestion. For instance, the
155 glycemic index (GI) of a bread depends on its density (d) (Saulnier, et al., 2010). A basic French baguette
156 ($d=0.16$) presented a GI of 75 whereas another one with identical composition but higher density
157 ($d=0.24$) presented a GI of 55, due to its lower starch accessibility. Indeed, GI is not considered a
158 characteristic of the human being but rather a property of the food item itself (ISO, 2010). Similarly,

159 the influence of food structure at various scales of pasta on the digestion of starch and proteins has
160 been extensively studied (M. Petitot, Abecassis, & Micard, 2009). The structure of cooked pasta is
161 generally described as a compact matrix with starch (a polymeric carbohydrate composed of amylose
162 and amylopectin) granules entrapped in a protein network. When heated in excess water, starch
163 granules absorb water and swell. This phenomenon, named gelatinization is caused by the disruption
164 of the native crystalline structure of starch granules. As granules continue to expand, amylose is
165 released from the intergranular phase to the aqueous phase. Cooling the gelatinized starch/water
166 mixture to room temperature induces the re-crystallization of starch molecules (mainly amylose); this
167 process is known as retrogradation. During digestion, the rate of starch hydrolysis in pasta is related
168 to various parameters. Among those, the degree of gelatinization and retrogradation of starch granule
169 and the amylose-to-amylopectin ratio seem to play a key role (Akerberg, Liljeberg, & Bjorck, 1998).

170 Pasta size (i.e. vermicelli vs. spaghetti) and shape (i.e. macaroni vs. spaghetti), which depend on the
171 forming step, seem also to be major factors, likely due to differences in surface-to-weight ratio leading
172 to differences in accessibility of amylase to starch (Granfeldt, Bjorck, & Hagander, 1991; Wolever, et
173 al., 1986). High pasta drying temperatures were shown to decrease the *in vitro* digestibility of starch
174 in cooked pasta (Maud Petitot, Brossard, Barron, Larré, Morel, & Micard, 2009). The hypothesis to
175 explain this phenomenon was high drying temperatures driving high levels of intermolecular protein
176 cross-linking, leading to more intense starch encapsulation, decreasing its susceptibility to enzymes.
177 Higher drying temperatures were also shown to decrease protein digestibility *in vitro* (Stuknyte, et al.,
178 2014). The higher resistance of proteins to digestion could be attributed to the presence of highly
179 aggregated proteins stabilized by covalent protein interactions, such as inter-peptide cross-linking and
180 Maillard-type aggregates (De Zorzi, Curioni, Simonato, Giannattasio, & Pasini, 2007).

181 Finally, studies have been conducted to demonstrate the effect of processing on the mechanisms of
182 nut digestion. A first set of experiments compared the *in vivo* kinetics of digestion of raw vs. roasted
183 almonds using the pig as a model, and showed that roasting decreased protein gastric emptying and
184 tocopherol bioavailability (Bornhorst, Roman, Rutherford, Burri, Moughan, & Singh, 2013). Proteolysis
185 was more intense in raw almonds, and some spatial differences were also observed with a higher
186 degree of proteolysis in the distal section of the stomach (Bornhorst, Drechsler, Montoya, Rutherford,
187 Moughan, & Singh, 2016). A study comparing the effects of boiling, roasting and frying peanuts found
188 that processing improved gastric disintegration of peanut particles by modifying their water absorption
189 and ultimately improving their softening (Kong, Oztop, Singh, & McCarthy, 2013)

190 These examples clearly show how processing modifies kinetics of macronutrient digestion. However,
191 structure differences in these examples occur mainly at molecular or supramolecular level (changes in
192 protein structure, aggregation, etc.), and there are fewer examples of comparisons between foods

193 with different macrostructures. In this context, the only way to really demonstrate the effect of food
194 structure on hydrolysis in the gastrointestinal tract is to compare the behavior of food of identical
195 composition and caloric charge but different macrostructure. To illustrate, six liquid, gelified or semi-
196 solid dairy matrices (skim raw or heat-treated milks, stirred and unstirred acid gel, raw or heat-treated
197 rennet gel) manufactured from the same milk powder (**Figure 2**) were given to six mini-pigs fitted with
198 two cannulas in the duodenum and mid-jejunum and equipped with a catheter in the abdominal aorta.
199 Gastric emptying half-time was shown to be directly influenced by food structure, at 98 min for the
200 liquid matrices increasing to 148 min for the acid gel (Le Feunteun, et al., 2014). Gel stirring led to an
201 intermediate viscous liquid structure and, consequently, to an intermediate gastric emptying half-time
202 of 124 min. Rennet coagulation significantly increased gastric emptying half-time. It was shown that
203 rennet gel was transformed into a dense curd in gastric conditions and that the curd was slowly eroded
204 by pepsin in the stomach, thus explaining the longer retention of the matrix in the stomach and the
205 dramatic increase in gastric emptying half-time (Barbe, Menard, et al., 2014). This definitively
206 demonstrates that at identical composition and caloric charge, food matrix structure regulates gastric
207 emptying. These data were obtained on pigs that are considered as the best model for mimicking the
208 upper part (i.e. stomach and small intestine) of the human tract (Kararli, 1995; Roura, et al., 2016).
209 Indeed, very similar trends were also observed in one of the only studies done on humans, where liquid
210 milk was found to empty more rapidly than yogurt (i.e. acid gel), thus modifying the kinetics of
211 proteolysis (Gaudichon, et al., 1995)

212 Quantification of milk proteins in the duodenal effluents showed significant between-sample
213 differences in kinetics of proteolysis in the small intestine (**Figure 3**). After ingestion of milk, caseins
214 and whey proteins massively and rapidly entered the duodenum, but after 30 mins their
215 concentrations quickly fell back down to basal levels. In contrast, acid gel led to a lower but much
216 longer-lasting increase of milk proteins than liquid milk (Barbe, et al., 2013). Similarly to gastric
217 emptying, stirred gel exhibited an intermediate behavior between milk and non-stirred acid gel. Finally,
218 rennet gel led to low concentrations of milk proteins throughout digestion with a slight increase after
219 7h of digestion, thus confirming the slow erosion by pepsin of the curd formed in the stomach (Barbe,
220 Menard, et al., 2014).

221 Quantification of plasma amino acids showed similar patterns to those observed for milk proteins in
222 the duodenum. For leucine (**Figure 4**), like the other amino acids, milk led to a sharp and early peak
223 whereas dairy gels led to a lower and later peak. Again, stirred gel showed an intermediate behavior
224 between milk and non-stirred gel, and rennet gel led to very low amino acid levels in the bloodstream.
225 Quantification of plasma ghrelin (**Figure 5**) showed a strong decrease in the hormone's concentration

226 in the hours following an acid gel ingestion compared to milk ingestion, indicating that acid gel
227 consumption could favor satiety.

228 Digestion of milk proteins is accompanied by the release of a myriad of peptides in the gut lumen. The
229 identification of these peptides showed that the pattern is also highly influenced by food structure. In
230 particular, the kinetics of appearance and disappearance of the peptides known to exert biological
231 activity (antimicrobial, immunomodulatory, anti-hypertensive, etc.) were shown to be different for the
232 six dairy matrices studied (Barbe, Le Feunteun, et al., 2014).

233 For lipids, we have used various structural approaches to control bioaccessibility. First, we tried to
234 modulate the interfacial layer of emulsion droplets. Indeed, type of emulsifier was previously reported
235 to influence lipid digestion *in vitro*, with lipid emulsifiers slowing digestion down compared to protein
236 emulsifiers (Mun, Decker, & McClements, 2007). We thus compared various processes of intestinal
237 digestion of triglyceride droplets (individual or in emulsion) stabilized by either a lipid emulsifier
238 (sodium oleate) or a protein emulsifier (β -lactoglobulin). Despite significant differences in the initial
239 mechanical properties of the interfacial layer, only minor effects emerged (Marze, 2015; Marze &
240 Choimet, 2012; Marze, Choimet, & Foucat, 2012). This was attributed to the adsorption of bile salts
241 desorbing most other molecules (except lipases) from the interface, thus lowering the mechanical
242 properties to the same values in both cases (Marze & Choimet, 2012). We also measured some
243 structural characteristics (including interfacial layer thickness) *in situ* using synchrotron small-angle X-
244 ray scattering, which showed that they were not significantly affected by emulsifier type throughout
245 intestinal digestion (Marze, Gaillard, & Roblin, 2015).

246 Another strategy to modulate the bioaccessibility of nutrients or micronutrients is to create a specific
247 bulk encapsulation structure. We tested a w/o/w double emulsion as a delivery system for betanin (a
248 hydrophilic betalain from red beet) during *in vitro* intestinal digestion (Kaimainen, Marze, Jarvenpaa,
249 Anton, & Huopalahti, 2015). In the digestion medium with no pancreatic lipase and no bile salt, the
250 double emulsion structures remained stable, so there was no betanin release from the inner water
251 droplets. In contrast, in the presence of pancreatic lipase and bile salt, betanin was released gradually
252 due to aggregation of w/o/w globules and coalescence of w/o inner water droplets as oil lipolysis
253 proceeded.

254 Other parameters (see the mathematical modeling section) and structures (McClements & Li, 2010)
255 should be tested to assess the potential of various emulsions as delivery systems in the context of
256 nutrition and satiety research (e.g. by accelerating lipid transit in order to trigger the ileal brake). One
257 of the next challenges is the digestion of more complex foods, where different types of nutrients are
258 released concurrently, possibly with synergistic or competitive interplays. For instance, proteolysis

259 kinetics strongly impacts the lipolysis kinetics of oil-in-water emulsions entrapped in a protein network,
260 whereas these reactions seem mainly independent when the same emulsion is dispersed in a liquid
261 protein solution (Mat, Le Feunteun, Michon, & Souchon, 2016). However, such variations in the
262 continuous emulsion phase may also influence gastric emptying kinetics, as evidenced for dairy
263 products, and/or possible lipid layering in the stomach. Unravelling the various effects of food
264 structure properties on digestion thus remains a challenging—but promising—area of research.

265

266 **Mathematical modeling of digestion; can we predict the physiological effect of food?**

267 The complexity involved in modeling the digestive process makes it an extremely ambitious goal. Food
268 digestion in the upper part of the gastrointestinal tract co-opts several mechanical (chewing in the oral
269 cavity, grinding and mixing in the stomach, etc.) and enzymatic (hydrolysis by digestive enzymes)
270 processes. Digestion can therefore be seen as a cascade of biological events that can be translated into
271 mathematical equations. Some human gastrointestinal tract models have been developed, making it
272 possible to integrate knowledge available on gut physiology and relationships between the different
273 organs involved (Liao, Zhao, & Gregersen, 2009). Some approaches have focused on one specific
274 compartment of the gastrointestinal tract. Computational modeling of the dynamics of gastric
275 digestion and fluid dynamics in the human stomach, for example, has focalized an intense and
276 innovative research effort (M. J. Ferrua & Singh, 2010; Maria J. Ferrua & Singh, 2011; M. J. Ferrua &
277 Singh, 2015). The data obtained underlines the complex interaction of food material properties and
278 physiological parameters that control the behavior of different digesta systems during gastric
279 digestion. Powerful retroulsive jet-like motions caused by the stomach contractions in the pylorus
280 area play a key role in suspending, breaking and dispersing gastric contents during digestion (Schulze,
281 2015)

282 Most of the *in silico* models available are compartmental models that take each independent section
283 of the gastrointestinal tract into consideration as well as the flows between them, and describe both
284 by a series of differential equations (Rivest, Bernier, & Pomar, 2000; Strathe, Danfaer, & Chwalibog,
285 2008; Wilson & Dainty, 1999). However, most of these models have never been validated against *in*
286 *vivo* data, and none of them take the structure and physical properties of food into account.

287 Our team recently developed a model of milk protein digestion and absorption using data collected
288 during the *in vivo* trial on mini-pigs with the 6 dairy matrices previously described in **Figure 2** (Le
289 Feunteun, et al., 2014). Data used to build the model were the duodenal concentrations of milk
290 proteins (**Figure 3**) and plasma amino acids (**Figure 4**). The model was purpose-constructed not only to
291 represent the main physiological events but also to account for several phenomena presumably

292 occurring within the stomach. We tested different behavioral hypotheses for each matrix, and only
293 selected the best model structures. A further originality of our model is that it accounts for the main
294 fluxes arising in the digestion process, thus enabling insight into quantities that were unobserved
295 during the original experiments, such as endogenous secretions, stomach volume or gastric emptying
296 kinetics. However, even though the model enabled progress in understanding the digestive process, it
297 is far from being predictive; for instance, it is impossible at this stage to predict the pattern of peptide
298 release in the gut lumen according to dairy product structure.

299 Some structural aspects of emulsified triglyceride digestion (namely bioaccessibility, the first step
300 towards bioavailability) were also modelled, using two approaches. One approach was based on multi-
301 agent simulation, reproducing the digestion processes at single triglyceride droplet scale (Marze, 2014,
302 2015). As this type of simulation relies on spatiotemporal and contact rules for different particles
303 (agents), it serves to test a host of situations. We were thus able to simulate the bioaccessibility kinetics
304 of lipophilic vitamins in a triglyceride droplet and investigate various parameters (structural,
305 compositional, digestive). We showed that lipophilic vitamin bioaccessibility is controlled by
306 triglyceride digestion, which is mainly influenced by triglyceride type, vitamin form (free vs. esterified),
307 and digestion conditions (*in vitro* vs. *in vivo*). Other parameters such as droplet size and gastric lipolysis
308 had less significant effects. Switching from increasing proportions of triglycerides to a non-digestible
309 oil (limonene) led to decreasing vitamin A bioaccessibility at a given digestion time, or to increasing
310 digestion times before reaching a given vitamin A bioaccessibility.

311 The other approach was based on mass transfer differential equations, serving to quantify the role of
312 most physical-chemical parameters (Marze & Choimet, 2012). The most important parameters were
313 initial droplet interfacial area and volume fraction, molar mass of the emulsified triglyceride, and the
314 mechanical properties of the interfacial layer. Zeroth-order and first-order kinetics equations were
315 derived. The most studied so far is the zeroth-order kinetics initially derived by Li & McClements (Li &
316 McClements, 2010) with an error, further corrected by Gaucel et al. (Gaucel, Trelea, & Le Feunteun,
317 2015). Both kinetics orders were found to suitably describe droplet digestion processes, but only a few
318 papers have evaluated their predictability according to their parameters. **Figure 6** illustrates the fitting
319 of two independent measurements of intestinal digestion of emulsified triglyceride by a first-order
320 kinetics equation, which was found to better represent the data than a zeroth-order one. In both cases,
321 the mass transfer coefficient was the only fitted parameter (Marze & Choimet, 2012).

322 We also developed a model of lipid hydrolysis that quantitatively reproduced the remarkable effect
323 the coalescence of oil droplets coalescence on their *in vitro* hydrolysis kinetics (Giang, et al., 2015).
324 This model has been further improved to predict kinetics of incorporation of all their constitutive fatty

325 acids within the bile salt micelles (**Figure 7**) (Giang, et al., 2016). Thanks to these promising results, we
326 are currently modeling the fate of fatty acids *in vivo*, from their ingestion through to their release into
327 blood plasma, using a dataset similar to the one obtained for proteins in mini-pigs. Our idea is to keep
328 a common basis with the model of protein digestion and absorption (secretions, transit, etc.) ready to
329 combine both models in the future. Long-term perspectives of this modeling strategy are to predict
330 more complex kinetics of food digestion by considering the postprandial fate of the different classes
331 of nutrients contained in a food or even a meal.

332 Performing clinical trials on animals and humans is getting increasingly difficult for ethical and
333 economic reasons. In turn, *in vitro* digestion models remain relatively limited for reproducing
334 physiological reality, which makes the challenge now to design *in silico* models to predict the fate of
335 food in the gastrointestinal tract.

336 **Reverse engineering: integrating our knowledge on food digestion to design new foods perfectly** 337 **adapted to human nutritional needs**

338 As described above, our knowledge of the precise mechanisms of food digestion has significantly
339 improved in the past few years. In particular, we now have a sharper picture of the way food structure
340 affects transit time in the different digestive compartments and the kinetics of macronutrient
341 hydrolysis. However, the physiological consequences of these differences of hydrolysis kinetics are still
342 unknown, and research is needed to determine whether the changes in kinetics of macronutrient
343 hydrolysis and nutrient bioavailability have an impact on human health. We do know that fast protein
344 hydrolysis allowing rapid release of branched-chain amino acids into the bloodstream can serve to
345 restore muscle protein synthesis in elderly people suffering from sarcopenia, i.e. aging-related muscle
346 loss (Rieu, et al., 2007). But are the benefits similar for other target populations, e.g. neonates or
347 healthy adults, or in pathologic cases? What about the other macronutrients (lipids, carbohydrates)?

348 The physiological consequences of a modification of residence time in the stomach are partly known.
349 For instance, it has been reported that slower gastric emptying tends to generate satiation and/or
350 satiety. It is therefore possible to develop a reverse engineering strategy in order to integrate this
351 knowledge and design foods whose structure will increase their residence time in the stomach. Since
352 dairy proteins are known to enhance satiety, two yogurts containing high levels of milk proteins (8 g
353 of protein/100 g yogurt instead of 3 g protein/100 g yogurt for a conventional product) were designed.
354 Both yogurts had exactly the same composition, but one had a high viscosity whereas the other had a
355 low viscosity. The gastric emptying half time of these 2 yogurts was estimated in pigs by gamma-
356 scintigraphy and compared to that of an iso-caloric yogurt enriched with starch. Yogurts were labeled

357 with technicium-99 and given to 12 conventional pigs (35 kg), and gastric emptying was followed by
358 gamma-scintigraphy during the first 3h after yogurt ingestion.

359 The results obtained (**Figure 8**) showed that gastric emptying was slowed down for the yogurts
360 enriched with milk proteins. Only the difference between the low-viscosity yogurt and the starch-
361 enriched control yogurt was statistically significant ($p < 0.05$), whereas the difference observed
362 between the high-viscosity yogurt and the control yogurt was not significant, likely due to higher
363 variability in the data obtained with the high-viscosity yogurt. The next step is to determine whether
364 these differences in gastric emptying time observed in pigs will generate satiety in humans.

365 A structural approach could also be used for lipids to let fatty acids reach the ileum (ileal brake), which
366 is known to slow down the whole GI transit process, inducing both satiation and satiety (Maljaars,
367 Peters, Mela, & Masclee, 2008). This could be achieved using delivery systems that initially accelerate
368 lipid transit and/or prolong their kinetics of release and, thus, their kinetics of absorption.

369 The transit time of a food in the gastrointestinal tract modulates the kinetics of its metabolism by the
370 body. Designing foods with controlled transit time would therefore allow better control of the kinetics
371 of nutrient availability and thus better fit the nutritional needs of specific populations. This will
372 probably be one of the key near-future challenges for the food industry to integrate these concepts
373 and move towards a more “personalized nutrition” for humans.

374

375 **Conclusion**

376 The past 10 years have seen a multidisciplinary scientific community composed of nutritionists, gut
377 physiologists and food scientists make significant progress to show that the fate of food in the
378 gastrointestinal tract depends, among other things, on the structure of the food matrix. Food cannot
379 be considered simply as an addition of proteins, lipids and carbohydrates. The way these constituents
380 are organized and interact with each other within the matrix affects the fate of food in the
381 gastrointestinal tract. It is therefore of paramount importance to integrate this new knowledge in
382 order to design food that is better adapted to the nutritional needs of specific populations, such as
383 infants, the elderly, and the overweight. Key to achieving this goal is to design food that is structured
384 to undergo modifications in the stomach that will make them more or less prone to disintegration, and
385 therefore modulate the kinetics of macronutrient hydrolysis and nutrient bioavailability. A joint effort
386 between academia and industry is required in order to reach this goal.

387

389

- 390 Akerberg, A., Liljeberg, H., & Bjorck, I. (1998). Effects of amylose/amylopectin ratio and baking
391 conditions on resistant starch formation and glycaemic indices. *Journal of Cereal Science*,
392 28(1), 71-80.
- 393 Akiba, Y., & Kaunitz, J. D. (2014). Duodenal Luminal Chemosensing; Acid, ATP, and Nutrients. *Current*
394 *Pharmaceutical Design*, 20(16), 2760-2765.
- 395 Armand, M., Pasquier, B., Andre, M., Borel, P., Senft, M., Peyrot, J., Salducci, J., Portugal, H., Jaussan,
396 V., & Lairon, D. (1999). Digestion and absorption of 2 fat emulsions with different droplet
397 sizes in the human digestive tract. *American Journal of Clinical Nutrition*, 70(6), 1096-1106.
- 398 Babusiak, M., Man, P., Petrak, J., & Vyoral, D. (2007). Native proteomic analysis of protein complexes
399 in murine intestinal brush border membranes. *Proteomics*, 7(1), 121-129.
- 400 Barbe, F., Le Feunteun, S., Remond, D., Menard, O., Jardin, J., Henry, G., Laroche, B., & Dupont, D.
401 (2014). Tracking the in vivo release of bioactive peptides in the gut during digestion: Mass
402 spectrometry peptidomic characterization of effluents collected in the gut of dairy matrix fed
403 mini-pigs. *Food Research International*, 63, 147-156.
- 404 Barbe, F., Menard, O., Le Gouar, Y., Buffiere, C., Famelart, M. H., Laroche, B., Le Feunteun, S.,
405 Dupont, D., & Remond, D. (2013). The heat treatment and the gelation are strong
406 determinants of the kinetics of milk proteins digestion and of the peripheral availability of
407 amino acids. *Food Chemistry*, 136(3-4), 1203-1212.
- 408 Barbe, F., Menard, O., Le Gouar, Y., Buffiere, C., Famelart, M. H., Laroche, B., Le Feunteun, S.,
409 Remond, D., & Dupont, D. (2014). Acid and rennet gels exhibit strong differences in the
410 kinetics of milk protein digestion and amino acid bioavailability. *Food Chemistry*, 143, 1-8.
- 411 Bornhorst, G. M., Drechsler, K. C., Montoya, C. A., Rutherford, S. M., Moughan, P. J., & Singh, R. P.
412 (2016). Gastric protein hydrolysis of raw and roasted almonds in the growing pig. *Food*
413 *Chemistry*, 211, 502-508.
- 414 Bornhorst, G. M., Roman, M. J., Rutherford, S. M., Burri, B. J., Moughan, P. J., & Singh, R. P. (2013).
415 Gastric Digestion of Raw and Roasted Almonds In Vivo. *Journal of Food Science*, 78(11),
416 H1807-H1813.
- 417 Bornhorst, G. M., & Singh, R. P. (2012). Bolus Formation and Disintegration during Digestion of Food
418 Carbohydrates. *Comprehensive Reviews in Food Science and Food Safety*, 11(2), 101-118.
- 419 De Zorzi, M., Curioni, A., Simonato, B., Giannattasio, M., & Pasini, G. (2007). Effect of pasta drying
420 temperature on gastrointestinal digestibility and allergenicity of durum wheat proteins. *Food*
421 *Chemistry*, 104(1), 353-363.
- 422 Efeyan, A., Comb, W. C., & Sabatini, D. M. (2015). Nutrient-sensing mechanisms and pathways.
423 *Nature*, 517(7534), 302-310.
- 424 Ferrua, M. J., & Singh, R. P. (2010). Modeling the Fluid Dynamics in a Human Stomach to Gain Insight
425 of Food Digestion. *Journal of Food Science*, 75(7), R151-R162.
- 426 Ferrua, M. J., & Singh, R. P. (2011). Understanding the fluid dynamics of gastric digestion using
427 computational modeling. *Procedia Food Science*, 1(0), 1465-1472.
- 428 Ferrua, M. J., & Singh, R. P. (2015). Computational modelling of gastric digestion: current challenges
429 and future directions. *Current Opinion in Food Science*, 4, 116-123.
- 430 Gaucel, S., Trelea, I. C., & Le Feunteun, S. (2015). Comment on New Mathematical Model for
431 Interpreting pH-Stat Digestion Profiles: Impact of Lipid Droplet Characteristics on in Vitro
432 Digestibility. *Journal of Agricultural and Food Chemistry*, 63(47), 10352-10353.
- 433 Gaudichon, C., Mahe, S., Roos, N., Benamouzig, R., Luengo, C., Huneau, J. F., Sick, H., Bouley, C.,
434 Rautureau, J., & Tome, D. (1995). Exogenous and endogenous nitrogen flow-rates and level
435 of protein hydrolysis in the human jejunum after [N-15]milk and [N-15]yogurt ingestion.
436 *British Journal of Nutrition*, 74(2), 251-260.

437 Giang, T. M., Gaucel, S., Brestaz, P., Anton, M., Meynier, A., Trelea, I. C., & Le Feunteun, S. (2016).
438 Dynamic modeling of in vitro lipid digestion: Individual fatty acid release and bioaccessibility
439 kinetics. *Food Chemistry*, 194, 1180-1188.

440 Giang, T. M., Le Feunteun, S., Gaucel, S., Brestaz, P., Anton, M., Meynier, A., & Trelea, I. C. (2015).
441 Dynamic modeling highlights the major impact of droplet coalescence on the in vitro
442 digestion kinetics of a whey protein stabilized submicron emulsion. *Food Hydrocolloids*, 43,
443 66-72.

444 Gonzalez-Arancibia, C., Escobar-Luna, J., Barrera-Bugueno, C., Diaz-Zepeda, C., Gonzalez-Toro, M. P.,
445 Olavarria-Ramirez, L., Zanelli-Massai, F., Gotteland, M., Bravo, J. A., & Julio-Pieper, M. (2016).
446 What goes around comes around: novel pharmacological targets in the gut-brain axis.
447 *Therapeutic Advances in Gastroenterology*, 9(3), 339-353.

448 Granfeldt, Y., Bjorck, I., & Hagander, B. (1991). On the importance of processing conditions, product
449 thickness and egg addition for the glycemic and hormonal responses to pasta - A comparison
450 with bread made from pasta ingredients. *European Journal of Clinical Nutrition*, 45(10), 489-
451 499.

452 ISO. (2010). ISO 26642-2010. Food Products - Determination of the Glycaemic index (GI) and
453 recommendation for food classification.

454 Kaimainen, M., Marze, S., Jarvenpaa, E., Anton, M., & Huopalahti, R. (2015). Encapsulation of betalain
455 into w/o/w double emulsion and release during in vitro intestinal lipid digestion. *LWT-Food
456 Science and Technology*, 60(2), 899-904.

457 Kararli, T. T. (1995). Comparison of the gastrointestinal anatomy, physiology, and biochemistry of
458 humans and commonly used laboratory -animals. *Biopharmaceutics & Drug Disposition*,
459 16(5), 351-380.

460 Kong, F. B., Oztop, M. H., Singh, R. P., & McCarthy, M. J. (2013). Effect of boiling, roasting and frying
461 on disintegration of peanuts in simulated gastric environment. *LWT-Food Science and
462 Technology*, 50(1), 32-38.

463 Le Feunteun, S., Barbe, F., Remond, D., Menard, O., Le Gouar, Y., Dupont, D., & Laroche, B. (2014).
464 Impact of the Dairy Matrix Structure on Milk Protein Digestion Kinetics: Mechanistic
465 Modelling Based on Mini-pig In Vivo Data. *Food and Bioprocess Technology*, 7(4), 1099-1113.

466 Lemmens, L., Colle, I., Van Buggenhout, S., Palmero, P., Van Loey, A., & Hendrickx, M. (2014).
467 Carotenoid bioaccessibility in fruit- and vegetable-based food products as affected by
468 product (micro) structural characteristics and the presence of lipids: A review. *Trends in Food
469 Science & Technology*, 38(2), 125-135.

470 Li, Y., & McClements, D. J. (2010). New Mathematical Model for Interpreting pH-Stat Digestion
471 Profiles: Impact of Lipid Droplet Characteristics on in Vitro Digestibility. *Journal of
472 Agricultural and Food Chemistry*, 58(13), 8085-8092.

473 Liao, D. H., Zhao, J. B., & Gregersen, H. (2009). Gastrointestinal tract modelling in health and disease.
474 *World Journal of Gastroenterology*, 15(2), 169-176.

475 Livny, O., Reifen, R., Levy, I., Madar, Z., Faulks, R., Southon, S., & Schwartz, B. (2003). beta-carotene
476 bioavailability from differently processed carrot meals in human ileostomy volunteers.
477 *European Journal of Nutrition*, 42(6), 338-345.

478 Macierzanka, A., Mackie, A. R., Bajka, B. H., Rigby, N. M., Nau, F., & Dupont, D. (2014). Transport of
479 Particles in Intestinal Mucus under Simulated Infant and Adult Physiological Conditions:
480 Impact of Mucus Structure and Extracellular DNA. *Plos One*, 9(4).

481 Maljaars, P. W. J., Peters, H. P. F., Mela, D. J., & Masclee, A. A. M. (2008). Ileal brake: A sensible food
482 target for appetite control. A review. *Physiology & Behavior*, 95(3), 271-281.

483 Marze, S. (2014). A coarse-grained simulation to study the digestion and bioaccessibility of lipophilic
484 nutrients and micronutrients in emulsion. *Food & Function*, 5(1), 129-139.

485 Marze, S. (2015). Refining in silico simulation to study digestion parameters affecting the
486 bioaccessibility of lipophilic nutrients and micronutrients. *Food & Function*, 6(1), 115-124.

487 Marze, S., & Choimet, M. (2012). In vitro digestion of emulsions: mechanistic and experimental
488 models. *Soft Matter*, 8(42), 10982-10993.

489 Marze, S., Choimet, M., & Foucat, L. (2012). In vitro digestion of emulsions: diffusion and particle size
490 distribution using diffusing wave spectroscopy and diffusion using nuclear magnetic
491 resonance. *Soft Matter*, 8(42), 10994-11004.

492 Marze, S., Gaillard, C., & Roblin, P. (2015). In vitro digestion of emulsions: high spatiotemporal
493 resolution using synchrotron SAXS. *Soft Matter*, 11(26), 5365-5373.

494 Mat, D., Le Feunteun, S., Michon, C., & Souchon, I. (2016). In vitro digestion of foods using pH-stat
495 and the INFOGEST protocol: impact of matrix structure on digestion kinetics of
496 macronutrients, proteins and lipids. *Food Research International*, 88, 226-233.

497 McClements, D. J., & Li, Y. (2010). Review of in vitro digestion models for rapid screening of
498 emulsion-based systems. *Food & Function*, 1(1), 32-59.

499 Mun, S., Decker, E. A., & McClements, D. J. (2007). Influence of emulsifier type on in vitro digestibility
500 of lipid droplets by pancreatic lipase. *Food Research International*, 40(6), 770-781.

501 Ng, M., Fleming, T., Robinson, M., Thomson, B., Graetz, N., Margono, C., Mullany, E. C., Biryukov, S.,
502 Abbafati, C., Abera, S. F., Abraham, J. P., Abu-Rmeileh, N. M. E., Achoki, T., AlBuhairan, F. S.,
503 Alemu, Z. A., Alfonso, R., Ali, M. K., Ali, R., Guzman, N. A., Ammar, W., Anwar, P., Banerjee,
504 A., Barquera, S., Basu, S., Bennett, D. A., Bhutta, Z., Blore, J., Cabral, N., Nonato, I. C., Chang,
505 J. C., Chowdhury, R., Courville, K. J., Criqui, M. H., Cundiff, D. K., Dabhadkar, K. C., Dandona,
506 L., Davis, A., Dayama, A., Dharmaratne, S. D., Ding, E. L., Durrani, A. M., Esteghamati, A.,
507 Farzadfar, F., Fay, D. F. J., Feigin, V. L., Flaxman, A., Forouzanfar, M. H., Goto, A., Green, M.
508 A., Gupta, R., Hafezi-Nejad, N., Hankey, G. J., Harewood, H. C., Havmoeller, R., Hay, S.,
509 Hernandez, L., Hussein, A., Idrisov, B. T., Ikeda, N., Islami, F., Jahangir, E., Jassal, S. K., Jee, S.
510 H., Jeffreys, M., Jonas, J. B., Kabagambe, E. K., Khalifa, S., Kengne, A. P., Khader, Y. S., Khang,
511 Y. H., Kim, D., Kimokoti, R. W., Kinge, J. M., Kokubo, Y., Kosen, S., Kwan, G., Lai, T., Leinsalu,
512 M., Li, Y. C., Liang, X. F., Liu, S. W., Logroscino, G., Lotufo, P. A., Lu, Y., Ma, J. X., Mainoo, N. K.,
513 Mensah, G. A., Merriman, T. R., Mokdad, A. H., Moschandreas, J., Naghavi, M., Naheed, A.,
514 Nand, D., Narayan, K. M. V., Nelson, E. L., Neuhouser, M. L., Nisar, M. I., Ohkubo, T., Oti, S. O.,
515 Pedroza, A., Prabhakaran, D., Roy, N., Sampson, U., Seo, H., Sepanlou, S. G., Shibuya, K., Shiri,
516 R., Shiue, I., Singh, G. M., Singh, J. A., Skirbekk, V., Stapelberg, N. J. C., Sturua, L., Sykes, B. L.,
517 Tobias, M., Tran, B. X., Trasande, L., Toyoshima, H., van de Vijver, S., Vasankari, T. J.,
518 Veerman, J. L., Velasquez-Melendez, G., Vlassov, V. V., Vollset, S. E., Vos, T., Wang, C., Wang,
519 X. R., Weiderpass, E., Werdecker, A., Wright, J. L., Yang, Y. C., Yatsuya, H., Yoon, J., Yoon, S. J.,
520 Zhao, Y., Zhou, M. G., Zhu, S. K., Lopez, A. D., Murray, C. J. L., & Gakidou, E. (2014). Global,
521 regional, and national prevalence of overweight and obesity in children and adults during
522 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*,
523 384(9945), 766-781.

524 Parada, J., & Aguilera, J. M. (2007). Food Microstructure Affects the Bioavailability of Several
525 Nutrients. *Journal of Food Science*, 72(2), R21-R32.

526 Petitot, M., Abecassis, J., & Micard, V. (2009). Structuring of pasta components during processing:
527 impact on starch and protein digestibility and allergenicity. *Trends in Food Science &*
528 *Technology*, 20(11-12), 521-532.

529 Petitot, M., Brossard, C., Barron, C., Larré, C., Morel, M.-H., & Micard, V. (2009). Modification of
530 pasta structure induced by high drying temperatures. Effects on the in vitro digestibility of
531 protein and starch fractions and the potential allergenicity of protein hydrolysates. *Food*
532 *Chemistry*, 116(2), 401-412.

533 Rieu, I., Balage, M., Sornet, C., Debras, E., Ripes, S., Rochon-Bonhomme, C., Pouyet, C., Grizard, J., &
534 Dardevet, D. (2007). Increased availability of leucine with leucine-rich whey proteins
535 improves postprandial muscle protein synthesis in aging rats. *Nutrition*, 23(4), 323-331.

536 Rivest, J., Bernier, J. F., & Pomar, C. (2000). A dynamic model of protein digestion in the small
537 intestine of pigs. *Journal of Animal Science*, 78(2), 328-340.

538 Roche, O.-. (2012). Enquête épidémiologique nationale sur le surpoids et l'obésité. 60 pp.

- 539 Roura, E., Koopmans, S. J., Lalles, J. P., Le Huerou-Luron, I., de Jager, N., Schuurman, T., & Val-Laillet,
540 D. (2016). Critical review evaluating the pig as a model for human nutritional physiology.
541 *Nutrition Research Reviews*, 29(1), 60-90.
- 542 Saulnier, L., Ducasse, M., Chiron, H., Della Valle, G., Martin, C., Issanchou, S., Rouau, X., & Rizkalla, S.
543 W. (2010). *Impact of texture modification and dietary fibre content on the glycemic index and*
544 *the acceptability of French bread*. Wageningen: Wageningen Acad Publ.
- 545 Schulze, K. S. (2015). The imaging and modelling of the physical processes involved in digestion and
546 absorption. *Acta Physiologica*, 213(2), 394-405.
- 547 Strathe, A. B., Danfaer, A., & Chwalibog, A. (2008). A dynamic model of digestion and absorption in
548 pigs. *Animal Feed Science and Technology*, 143(1), 328-371.
- 549 Stuknyte, M., Cattaneo, S., Pagani, M. A., Marti, A., Micard, V., Hogenboom, J., & De Noni, I. (2014).
550 Spaghetti from durum wheat: Effect of drying conditions on heat damage, ultrastructure and
551 in vitro digestibility. *Food Chemistry*, 149, 40-46.
- 552 Turgeon, S. L., & Rioux, L. E. (2011). Food matrix impact on macronutrients nutritional properties.
553 *Food Hydrocolloids*, 25(8), 1915-1924.
- 554 Tydeman, E. A., Parker, M. L., Faulks, R. M., Cross, K. L., Fillery-Travis, A., Gidley, M. J., Rich, G. T., &
555 Waldron, K. W. (2010). Effect of Carrot (*Daucus carota*) Microstructure on Carotene
556 Bioaccessibility in the Upper Gastrointestinal Tract. 2. In Vivo Digestions. *Journal of*
557 *Agricultural and Food Chemistry*, 58(17), 9855-9860.
- 558 Vors, C., Pineau, G., Gabert, L., Drai, J., Louche-Pelissier, C., Defoort, C., Lairon, D., Desage, M.,
559 Danthine, S., Lambert-Porcheron, S., Vidal, H., Laville, M., & Michalski, M. C. (2013).
560 Modulating absorption and postprandial handling of dietary fatty acids by structuring fat in
561 the meal: a randomized crossover clinical trial. *American Journal of Clinical Nutrition*, 97(1),
562 23-36.
- 563 WHO. (2013). Global Health Observatory - World Health Statistics. 172 pp.
- 564 Wilson, P. D. G., & Dainty, J. R. (1999). Modelling in nutrition: an introduction. *Proceedings of the*
565 *Nutrition Society*, 58(1), 133-138.
- 566 Wolever, T. M. S., Jenkins, D. J. A., Kalmusky, J., Giordano, C., Giudici, S., Jenkins, A. L., Thompson, L.
567 U., Wong, G. S., & Josse, R. G. (1986). Glycemic response to pasta - Effect of surface-area,
568 degree of cooking, and protein enrichment. *Diabetes Care*, 9(4), 401-404.

569

570

571

572 **Figure captions**

573

574 **Figure 1.** Understanding the fate of food in the gastrointestinal tract to design new foods by reverse
575 engineering.

576 **Figure 2.** Design of six iso-caloric dairy matrices of identical composition but different microstructure.

577 **Figure 3.** Evolution of β -lactoglobulin (left) and casein (right) concentrations as measured in the
578 duodenum of 6 mini-pigs fed a heated milk, acid gel, stirred acid gel and rennet gel of identical gross
579 composition.

580 **Figure 4.** Evolution of leucine concentration in plasma of mini-pigs fed a heated milk, acid gel, stirred
581 acid gel and rennet gel of identical gross composition.

582 **Figure 5.** Evolution of ghrelin concentration in plasma of mini-pigs fed a heated milk, acid gel, stirred
583 acid gel and rennet gel of identical gross composition.

584 **Figure 6.** Fatty acid release during *in vitro* intestinal digestion monitored by pH-stat (dotted line),
585 modeled by first-order kinetics including a solubility parameter (full line). Mass transfer coefficient and
586 bioaccessibility are fitted. Emulsions of triolein stabilized by β -lactoglobulin (pink) or sodium oleate
587 (green) or emulsions of tricaprylin stabilized by β -lactoglobulin (red) or sodium oleate (black).

588 **Figure 7.** Comparison between modeled and experimental time-course of the bioaccessibility of
589 individual lipolysis products (i.e. contained within the bile salt micellar phase) during *in vitro* intestinal
590 digestion. Symbols are means \pm sd over 3 replicated digestion experiments, and solid lines represent
591 the model simulations.

592 **Figure 8.** Gastric emptying of yogurts enriched in low-viscosity and high-viscosity proteins and an iso-
593 caloric placebo

594

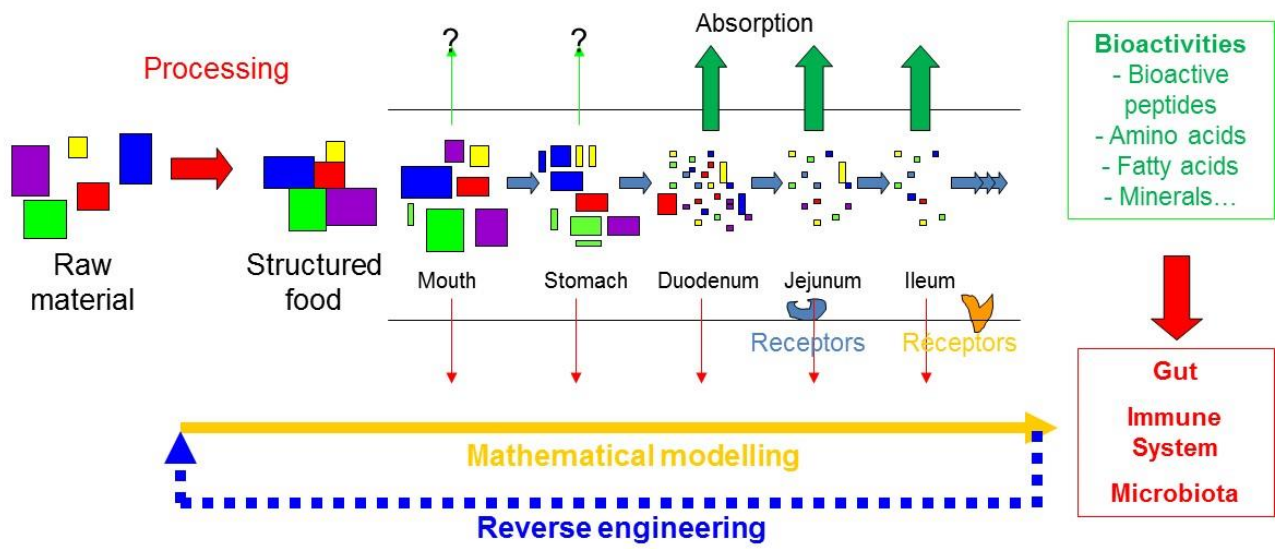


Figure 1

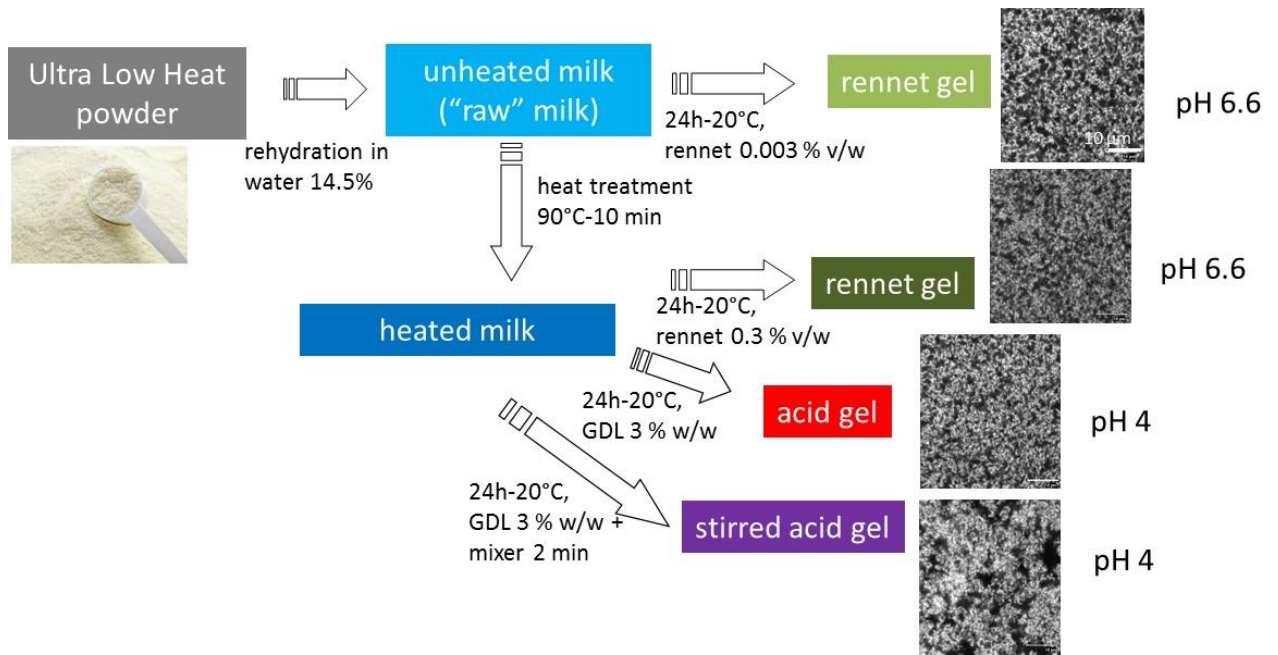


Figure 2

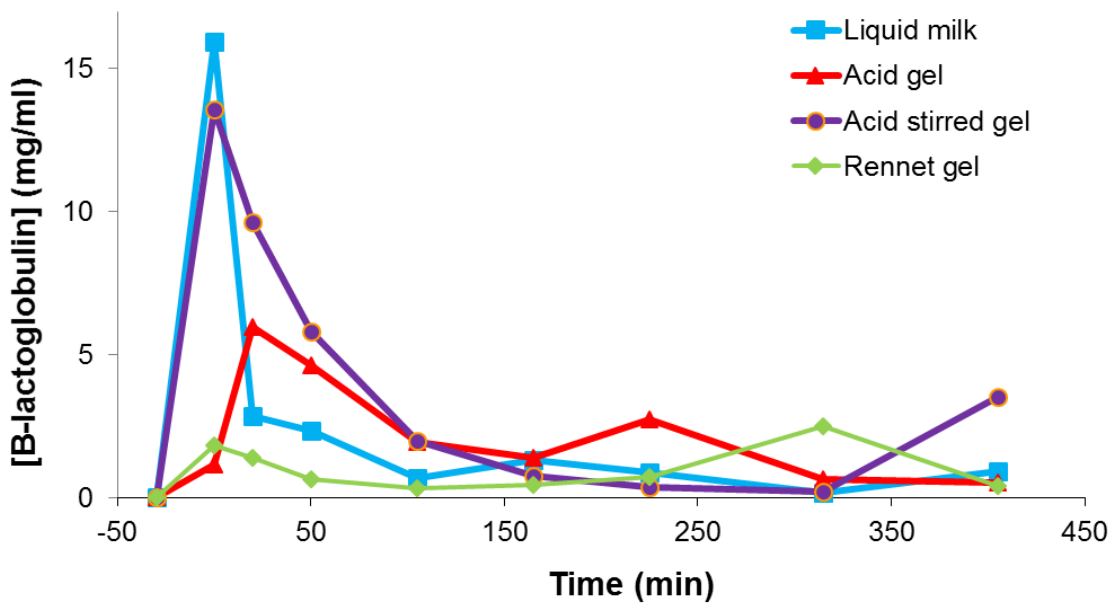
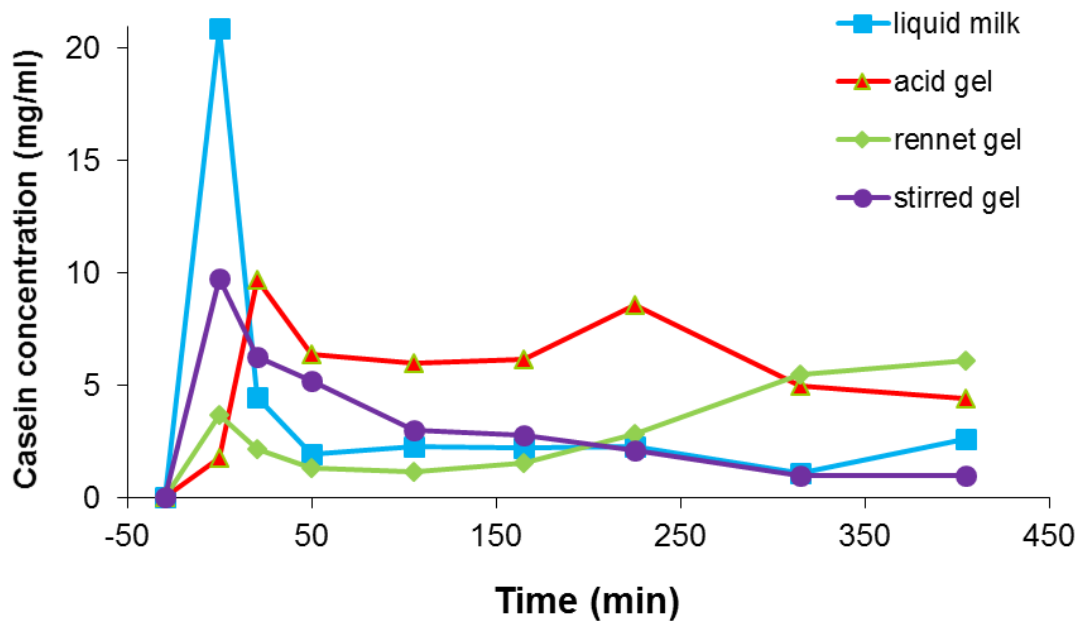


Figure 3

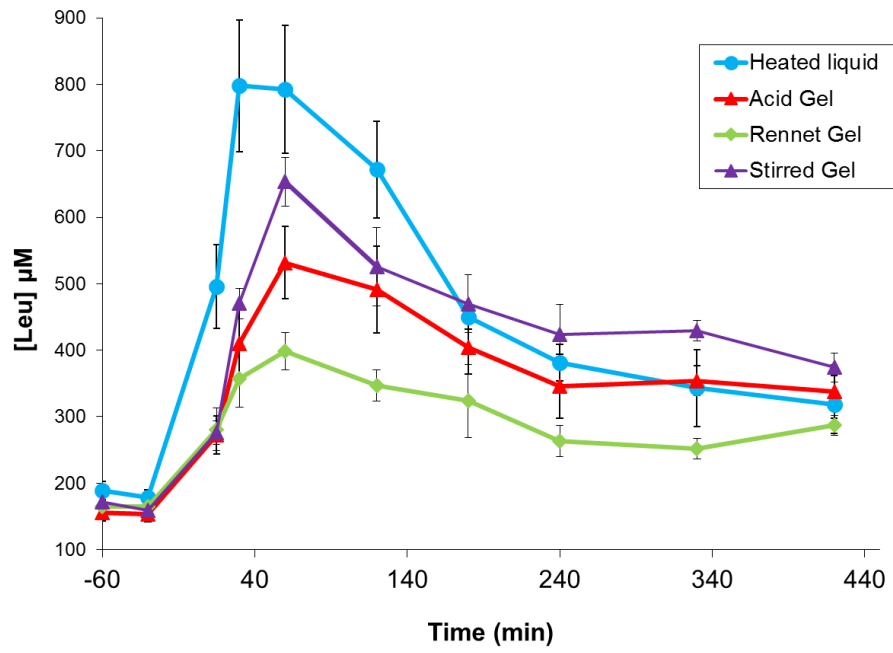


Figure 4

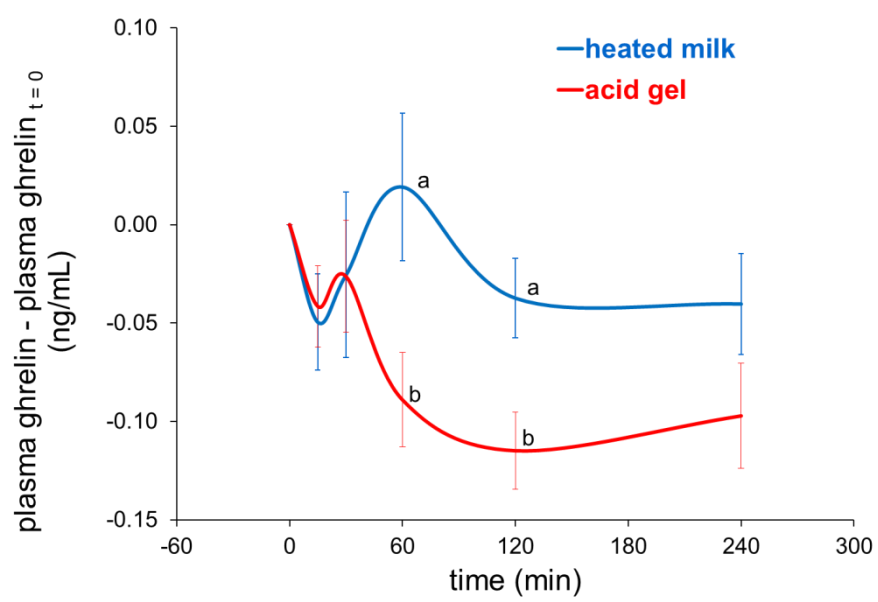
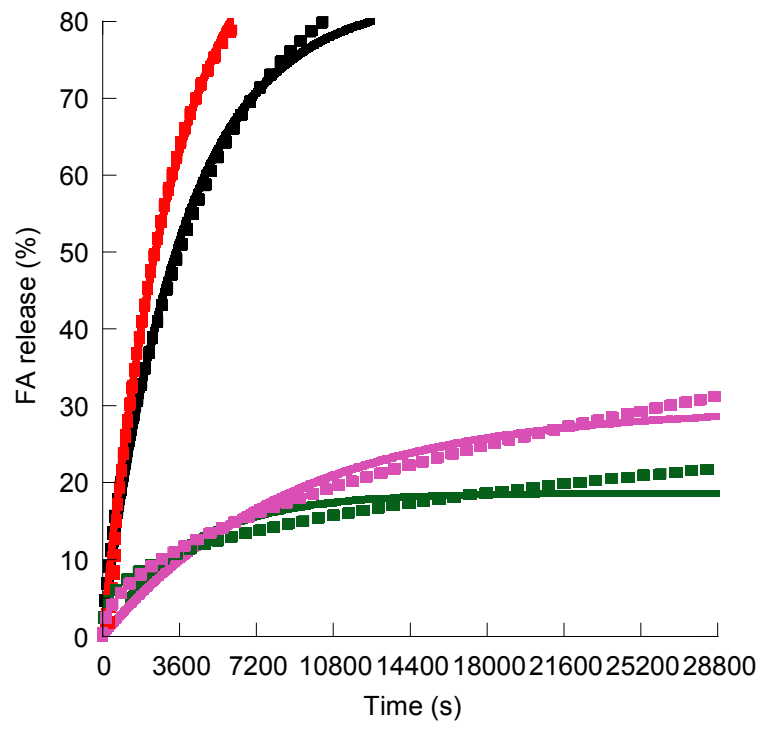


Figure 5



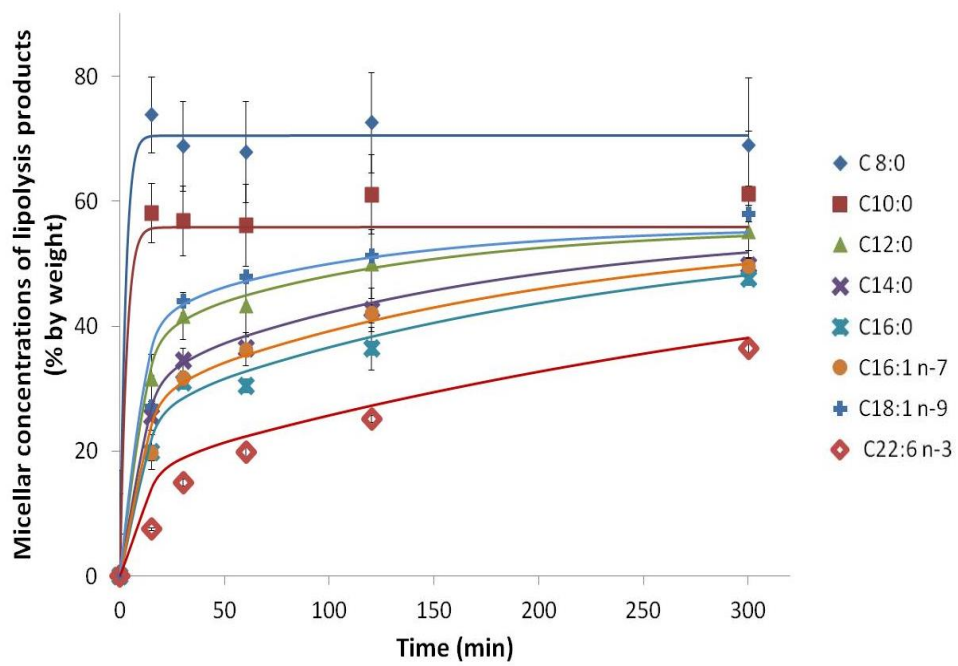


Figure 7

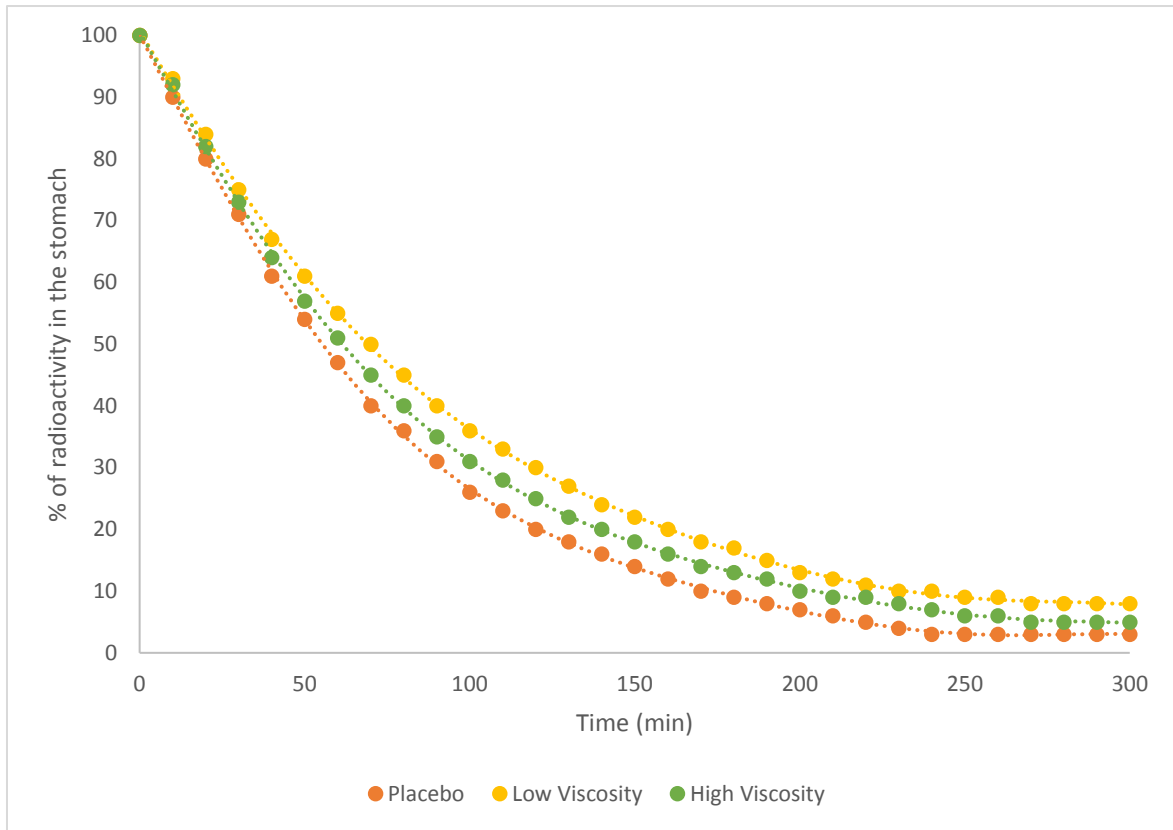


Figure 8