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Abstract

Background*:** The complexity of food structure is such as to hinder its inclusion in mathematical models predicting food properties and transformations, although a considerable impulse is being determined by using artificial intelligence. As a matter of fact, food definition currently neglects the structural description, even in those fields for which structure is demonstrated to have a decisive role, such as nutrition. ***Scope and approach: This review aims to analyse the current knowledge about the structure of foods and its potential use to numerically define the sensory and nutritional quality, as well as the stability properties. Starting from this information, a possible methodology is explored to build, even in an automated way, mathematical models for simulating and predicting the properties of food. A model pipeline has been proposed and applied to pasta, in particular exploiting the description of the structural changes occurring upon cooking. ***Key findings and conclusions:*** Foods may be designed *in silico*, based on automated pipelines for direct extraction of information on rheological and sensory properties as derived from structure images and from data on the dynamic state of the water. The ultimate goal of these approaches is to make more limited use of expensive and time-consuming experiments on physically prepared foods to get to use digital twins of foods designed in the laboratory.

Key words: food structure; bio-accessibility; bioavailability; functional food; digital twin; *in silico* food; digestion.

1. Introduction

Although the description of food has traditionally been based on analytical chemical composition, many of the important properties of food are determined by structural elements. This limitation in the descriptive capacity of a food is also reflected in many mathematical models that currently aim to predict the sensory, functional, and nutritional properties, including for example digestibility. For this reason, the contribution of the structure of a food is often overlooked including when studying the effect of diet on health. In fact, the nutritionist tends to consult compositional databases when the correctness of a diet must be evaluated, having no indication on how to use any structural data even when available. Nevertheless, before collecting structural information, it would be necessary to establish how to use them to build predictive models for nutritional functions that depend on it. Understanding how the ingredients and each unit operation of food processes make up the structure of the foods and how this structure changes during its life or on eating will play a main role in the development and management of the food science and industry. For this reason, a tailored collection of scientific work described in the literature has been examined to pave the way for a future approach using matrix structural data to predict food functions, also exploiting artificial intelligence (AI).

2. What is the structure of a food?

Most foods are complex, heterogeneous materials composed of structural elements or domains (co-) existing as solids, liquids and/or gases, where length scales span nanometres to millimetres (Guo, Ye, Bellissimo, Singh, & Rousseau, 2017). Many of the important properties of foods are determined by structural elements of micro-scale and above, such as bubbles, drops, strings and particles (Ubbink, Burbidge, & Mezzenga, 2008). Food products consist largely of carbohydrates, proteins, and lipids, forming clusters that behave as pseudo-molecules of higher molecular weight than the individual constituent molecules (Ubbink, et al., 2008). These interactions are primarily hydrogen-bonding interactions between the hydroxyl groups or Van der Waals interactions between nonpolar molecules, but also ionic or covalent bonds, such as disulphide or isopeptide, may be very important. The supramolecular organization of foods gives rise to their structure. Complex food structures are formed, not because of the abundance of elemental components, but because of the multiple interactions that proteins, lipids and polysaccharides undergo at different conditions in an aqueous medium.

In natural and processed foods, the structure (or matrix) of a food is defined as the organization of its constituent molecules at multiple spatial length scales (Guo, et al., 2017). At one extreme, a food product is macroscopic, and at the other extreme, it is composed of molecules and atoms

characterized by molecular length scales (Ubbink, et al., 2008). The matrix of a food is in fact scale-sensitive, i.e., interactions may take place at several scales in the same food as shown in Figure 1.

For example, the matrix in a bakery product responsible for the textural properties of the porous crumb are the protein-starch walls surrounding the air cells (Aguilera, 2019), and the relevant scale is on the order of a few hundred microns (Liu & Scanlon, 2003). Starch granules undergoing gelatinization may be regarded as inclusions in the continuous gluten matrix at a scale of approximately 10 μm (Maeda, et al., 2013). At the nanoscale, gelatinized starch granules are the matrix onto which a-amylases exert their action during digestion to release glucose molecules (Li, Yu, Dhital, Gidley, & Gilbert, 2019). By and large, foods are systems of dispersed phases, such as mesoscale particulate structures (colloids) derived from natural food products constructed by self-assembly (e.g., granules, micelles, globules, and fibres) or are created artificially via food processing (R. Van der Sman & Van der Goot, 2009). Next to these mesoscale structures, food contains smaller molecular species, like salts, sugars, polyols and phospholipids, which moderate the properties of the continuous or dispersed phases, or their interfaces. The structure of a given food depends, however, enormously on the product, its constituents and which of the many length scales are dominant in establishing the product properties (Ubbink, et al., 2008). For an emulsion-based food such as mayonnaise, it is the droplet size of around 1μm which is the relevant length scale, whereas for dairy products it is typically the size of a casein micelle (~50-100 nm) (de Kruif & Huppertz, 2012) and the size of the individual casein subunits (~2 nm) that matter. The relevant length scale of food powders is typically between 10 and 500 μm, and the structure of starch is described at length scales between the macromolecular (~1 nm) and the size of the starch granules (~1 mm). Even length scales substantially smaller than 1 nm matter in foods, as diffusion and the interaction of water with the food matrix occur at these distances.

Food structure is important at all dimensional scales for texture, sensory properties, shelf life and stability and can alter the kinetics and extent of food digestion (Guo, et al., 2017; H. Singh, Ye, & Horne, 2009). It plays a vital role in how food interacts with the gastrointestinal tract (GIT) (e.g., bodily fluids and receptors) and the resulting release and uptake of nutrients (Guo, et al., 2017) and post-prandial outcomes (Turgeon & Rioux, 2011) In addition, the breakdown of the food matrix is a major controlling factor for the perception of texture and flavour in the mouth (Harjinder Singh, Ye, & Ferrua, 2015).

3. How to quantitatively measure food structure

Several techniques can be applied to measure the structure of food materials either directly (optical and confocal microscopy, tomography, scanning and electron microscopy) or indirectly from measurements of the mechanical response or spectroscopy (Table 1). Some challenging techniques such as Differential Scanning Calorimetry (DSC) (Tester & Debon, 2000; Zhu, Zhou, & Sun, 2019), Thermogravimetric analysis (TGA) (Tavares, Santos, & Noreña, 2021), Nuclear Magnetic Resonance (NMR) spectroscopy and relaxometry (Kirtil & Oztop, 2016), Near-Infrared Reflectance spectroscopy (NIR) (Shi, Lei, Louzada Prates, & Yu, 2019), Attenuated Total Reflectance (ATR) spectroscopy (Cebi, Durak, Toker, Sagdic, & Arici, 2016) and FT-Raman spectroscopy provide quantitative parameters that are related to the interactions among molecules, thus making measurable physical-chemical properties that depend on the supramolecular structure of the food matter. However, imaging techniques are essentially dedicated to the investigation of the real 3D structure (Falcone, et al., 2006). Static Bragg-type diffraction of neutrons and X-rays has been applied to either fluid or viscous food systems to reveal the structure in the 10–100 nm length scale range (Ubbink, et al., 2008). Insight into lipid polymorphism, liquid crystallinity, protein folding, etc. can typically be gained by using these techniques. Because most common food properties are, however, directly related to the μm length scale, light scattering techniques are primarily exploited. The application of the dynamic light scattering (DLS) experiment to foods yields information on the diffusion coefficient of the scattering objects (Ubbink, et al., 2008). Tomographic techniques such as magnetic resonance imaging (MRI) and X-ray tomography are extremely powerful since they allow a full 3D reconstruction of the sample structure but tend to be limited in resolution and/or slow in acquisition times. Optical or Light Microscopy (LM) suffers from a similar limitation in resolution, in this case due to the wavelength of visible light, even though structures of the order of 1 μm can still be imaged using confocal microscopy. A further limitation of optical techniques is that the food sample should be sufficiently transparent. Conversely, a major advantage of optical microscopy is that dynamic processes on time scales larger than about 10 ms can easily be followed (Ubbink, et al., 2008). In the imaging of samples using transmission electron microscopy (TEM), special staining, embedding and cutting techniques are indispensable, whereas the use of scanning electron microscopy (SEM) is much more straightforward (García-García, Cambero, Castejón, Escudero, & Fernández-Valle, 2019). An interesting development is the progress in so called environmental scanning electron microscopy (ESEM), which allows the analysis of samples at a desired relative humidity and thus avoids artifacts due to the dehydration of foodstuffs (Ubbink, et al., 2008).

Different methods for image acquisition (light microscopy, transmission electron microscopy and scanning electron microscopy) are generally coupled to digital analysis to quantitatively define, with structural parameters, food at different structural levels. This provides a measurement of different aggregation descriptors. The gel network can be characterized by structural parameters such as pore size, strand dimensions and how these are distributed in the volume. In the case of particulate gels, the diameter size of the pore is large, up to hundreds of microns, compared to the size of the particle, around microns (Langton & Hermansson, 1996). At low magnifications LM is used to estimate the size of the large pores. At higher magnifications TEM estimates the size of the particles forming the strands of networks. The pore size is more easily measured by digital image analysis than by evaluating the difference in aggregation of particles in the network. In SEM the fracture plane is visualized, and the fracture will follow the weakest structure, i.e., large pores. Thus, SEM micrographs tend to show larger pores. and smaller pores could be embedded in clusters or conglomerates. Stereology is a tool for measuring complex biopolymer gels, where no assumptions of the shape can be made. A stereological approach was used to classify the mode of aggregation by a group of experienced microscopists evaluating SEM-micrographs, to quantify pore size, particle size and amount of threads within the pores in volume weighted mean volumes (Langton & Hermansson, 1996). Five structural descriptors were quantified, namely porosity (number of pores), clusters (many particles attached to each other like bunches of grapes), conglomerates (as if the particles were joined together in non-linear, irregular, inhomogeneous order), strings of beads (as if the particles were attached to each other in a linear order forming strings of beads) and hairiness (as if small threads were attached to the surface of the particles and their outline is indistinct). The three-dimensional gel network is responsible for bulk properties such as diffusion and rheological properties, sensory quality and liquid holding capacity (Langton & Hermansson, 1996).

4. The properties the food structure affects: sensory, stability, digestibility and bioaccessibility

The dimensions/size and shape/form of the particles, strands and pores create the different textural properties of the food products and expert panellists can detect differences between very small particles <1 μm^3 in volume (Langton, Åström, & Hermansson, 1997). In fact, texture is a multi-parameter attribute, that derives from the molecular, microscopic or macroscopic structure of a food and is detected by several senses, the most important ones being the senses of touch and pressure (Szczesniak, 2002). Food structure, food texture, nutrients digestibility

and consumer product preferences and choices are intrinsically linked (Figure 1). Texture influences people's acceptance of food and may be more important than the flavour in some products (Clark, 1998). The sensory perception during food consumption depends not only on the concentrations of odour- and taste-active compounds but also on the texture of food matrix (Tournier, Sulmont-Rossé, & Guichard, 2007).

Multivariate techniques are used to create models to describe groups of the sensory descriptors by some of the microstructural parameters (Janhøj, Frøst, & Ipsen, 2008; Pereira, Singh, Munro, & Luckman, 2003). Correlations between the microstructure and sensory descriptors have been found: grainy appearance, gritty texture, creamy texture and tendency to fall apart have a logarithmic dependence on the particle size, and size of small and large pores (Langton, et al., 1997). The soft and springy textures are influenced by combinations of microstructural parameters, where the formation of strands into strings of beads or in clusters and conglomerates seems to play an important role. Conversely, the sticky texture is negatively correlated to the proportion of threads within the pores (Langton, et al., 1997). Stability can be fully grasped only if food molecular dynamics and structure are taken into consideration, i.e., an appropriate understanding of the behaviour of food products requires knowledge of its composition, structure and molecular dynamics, through the three-dimensional arrangement of the various structural elements and their interactions (Wu, et al., 2020). In addition to water, other structural elements can be identified in foods at a supramolecular structure level, such as oil droplets, gas cells, fat crystals, strands, granules, micelles and interfaces. These structural elements, composed of proteins, carbohydrates and lipids (in various combinations and proportions), can exist in different states (glassy/rubbery/crystalline/liquid and solubilised) even at uniform temperatures and water activity. This structural heterogeneity will necessarily affect the molecular dynamics in the system and consequently the macroscopic food quality attributes and their behaviour along storage. Physically separating the reactants in microstructural locations can control the biochemical activity by avoiding the reactants to be in contact.

It is a matter of fact that the gastrointestinal fate of lipids depends on their level, type, and structural organization in foods (McClements, 2018). Matrices could be formed by controlled gelation of single or mixed biopolymer systems around lipid droplets, by dehydration of oil-in-water emulsions containing biopolymers or other wall materials, or by thermal treatment or extrusion of starch matrices containing lipid droplets. Several studies have recently investigated the impact of the food matrix on the digestibility of lipids using either *in vitro* or *in vivo* digestion models (Corstens, et al., 2017; Dias, Zhu, Thompson, Singh, & Garg, 2019; J. Singh,

Dartois, & Kaur, 2010). When oil droplets are dispersed in a solid-like food matrix (e.g., cheese or strained-type yogurt), the structure of the surrounding food matrix becomes the dominant factor controlling digestion. For instance, the size of lipid droplets dispersed of oil-in-water emulsions and nano emulsions can affect, during digestion, oil-soluble vitamins (vitamins A, D, E and K) bioavailability in fortified foods (Tan & McClements, 2021); increasing oil droplet size reduces the bioaccessibility by inhibiting lipid digestion and reducing micelle solubilisation (Tan, Zhang, Liu, Xiao, & McClements, 2020). The knowledge advances provided by these studies are setting the foundation for modulating fat digestion through food structure design, as exhaustively reviewed by Guo, et al. (2017). In this sense, food structure design can be a tool to develop foods that enable to control the body district as well as the extent and rate of release of food lipids along the digestion process.

During digestion, the 3D network structure within a food matrix can obstruct the diffusion of enzymes towards the surface of dispersed oil droplets. That is the reason why bile salts are produced by the intestinal tract and released during food digestion to create an emulsion where the digestive enzymes can act onto the food lipids.

Compared to interfacial films, the solid like-food matrix is potentially capable of providing enhanced protection against lipolysis (Guo, et al., 2017). Evidence is accumulating that a structured food with a high protein content may show slower lipid digestion (Salentinig, 2019). An investigation on near forty food types, based on the harmonized INFOGEST digestion method (Brodkorb, et al., 2019), found that those with medium and low lipid content showed a limited lipolysis extent when the content of protein or starch was high (Calvo-Lerma, Fornés-Ferrer, Heredia, & Andrés, 2018). In protein-rich foods such as cheese, the disintegration of the protein network occurs mainly in gastric and intestinal steps, thus facilitating the subsequent release of fat aggregates from the degraded matrix (Žolnere, Arnold, Hull, & Everett, 2019). These results underline the importance of microstructure and the digestive environment on the release of cheese components.

The *in vitro* digestion rate of lipids and starch was also reduced due to the intact vegetal cell walls (Dhital, Bhattarai, Gorham, & Gidley, 2016). The intact cell wall structure and protein matrices are impervious to amylase and can prevent or slow down enzyme diffusion to substrate. In general, the intactness of cell walls is related to particle size, which is dependent on mastication habits and processing conditions, for example, milling and heating (Li, Gidley, & Dhital, 2019). The hydrolysis of intracellular starch and protein in the essentially intact cells was 2–3%, whereas this increased to 40–45%, when the cells were mechanically broken and digested, suggesting a barrier effect of intact cell walls to digestive enzyme access to starch and

proteins substrate (Ogawa, et al., 2018). In support to this hypothesis, it has been shown that solubilisation of pectin cell walls, induced by thermal treatment of bean, exerted higher degrees of cell wall permeability so that starch hydrolysis increased proportionally to the cell damage (Pallares, et al., 2018). The morphology and the particle size of starch granules from different plants is also considered an important factor affecting their digestion, as smaller granules have greater enzymatic susceptibility regardless of botanical origin, due to their larger specific surface area (Lehmann & Robin, 2007; Romano, et al., 2018; Romano, et al., 2016). Moreover starch granules vary in the level of porosity and can have openings (pores) on the surface of the granule (Fannon, Hauber, & Bemiller, 1992).

During processing, starch granules swell and lose their crystallinity and molecular organization in a process commonly known as gelatinization. *In vitro* studies have demonstrated that the rate of enzyme breakdown of gelatinized starch is much higher than that of native starch; native wheat starches are degraded by only 10–15%, but after partial gelatinization the rate of enzymatic degradation increased three-fold (Tian, et al., 2019). Therefore, gelatinization may strongly influence the rate at which starch is digested and elicits the glycaemic response.

Starch–protein interaction in white flours might account for a decrease in *in vivo* glycaemic response as well as for a reduction in *in vitro* digestibility, so that the removal of gluten from wheat flour induces a high GI value in 11 kinds of gluten-free bread. In addition to acting as an enzyme barrier, proteins also affect the properties of starch (gelatinization, retrogradation, etc.) which is then less digestible (de la Hera, Rosell, & Gomez, 2014). If proteins are present in a structured matrix or a clot-like structure is formed in the gastric environment, gastric juice needs to penetrate this structured matrix to digest the protein. A 2–10 reduction factor for the diffusion coefficient of pepsin has been measured in a structured matrix as compared to water. The diffusion of pepsin is one of the limiting factors in the digestion rate of a structured food matrix (E. Capuano & A. E. M. Janssen, 2021). Different egg-white gel structures, with a similar protein composition, induced different proteolysis kinetics and provoked the release of different specific peptides (Nyemb, et al., 2016).

Proteins can form supramolecular assemblies also because of thermal treatment. The formation of aggregates may hide peptide bonds from proteases compared to denatured but isolated molecules. The effect of cooking on the digestibility of meat proteins is a good example of such complex relationships. Meat digestibility of regular-cooked beef was higher (95% digested) than that of ‘well-done’ cooked beef (90% digested). Meat analogues are a class of food products that imitate the sensory attributes of meat products but are produced from protein from more sustainable sources, e.g., plant protein isolates, that are subjected to extrusion or shear-

cell technology. In these products, the presence of other food ingredients or components, such as lipids and polyphenols, may affect protein digestibility. These effects are still poorly understood for the lack of knowledge of the matrices and by the absence of predictive models. Therefore, in the design of novel foods the effects of components on protein digestibility should be carefully considered in the optimization of the processing parameters (E. Capuano & A. E. Janssen, 2021). The process-induced modifications, *in primis* the Maillard reaction, could also play a role in modulating the food digestibility and the bioavailability of protein amino acids, by altering the chemical structural of protein networks and in turn the food microstructure: this is the case of bread, dairy and meat products. Not secondarily, these modifications can also affect the food allergenicity, through the interactions of protein-bound advanced glycation end-products (AGE) with immune cells receptors, as evidenced for egg, dairy and peanut allergens (Mueller, et al., 2013; Teodorowicz, Van Neerven, & Savelkoul, 2017; Toda, Hellwig, Henle, & Vieths, 2019).

5. The importance of structure in food design: driver for functional foods?

The main objective of the food industry is to create products with specific properties and characteristics which have a positive consumer impact. In recent years, the food industry, aware of resource scarcity, is looking for nutritional alternatives, including functional foods, that promote optimal health and help reduce the risk of disease and are "tailored". Tailoring is a process whereby the provision of information, advice and support is individualized to the user (Lustria, et al., 2013). Mimic foods to be substituted, include also new functional ingredients in formulation. The attempt to design new foods starting from more sustainable or more nutrient-rich ingredients, with optimal characteristics for target population groups with specific needs, has always clashed with the need to make these new foods at least as palatable, if not preferable, to traditional ones. The limit is often in the obtainment of a desirable structure. In fact, unlike some homogeneous foods, such as drinks, extracts or oils, most foods are heterogeneous multiphase mixtures, having nutritional and sensory characteristics that strongly depend on the placement with which the different phases are distributed in space, while forming the food matrix. For this reason, the food technologists make use of structure-targeted toolboxes to mimic successful matrices or invent new ones with even more performing characteristics. This is usually carried out empirically in lab scale plants but, to avoid prolonged and expensive physical research trials, the structure of the food could be preliminarily built *in-silico* also in the design phase. This effective approach could be realized using conceptual toolboxes (simulating unit operations, order of sequential steps, formulations) assisted by mathematical

prediction models. The purpose of designing the most suitable structures is then fulfilled, through combinations of formulations and processes, to achieve the desired outcomes, like the optimized durability, palatability, bioaccessibility and bioavailability of nutrients. This way, food design considers not only composition, but also structure affecting chemical stability, texture and dynamics of digestion and absorption of a food or its components. In this perspective, tailored foods provide not only the necessary nutrients but also new functions, linked to the matrix structure, targeted for specific populations groups such as the elderly, babies, athletes, allergic peoples, vegans or for special diets such as low salt, sugars and fats, or lactose- and gluten-free, and to increase the quantity of proteins, vitamins, dietary fibres, and bioactive phytochemicals. Designer-made supramolecular food materials may form the basis for personalized, health-promoting diets of the future (Norton, Espinosa, Watson, Spyropoulos, & Norton, 2015). As already described in the previous section (Table 1), foods are made by colloids toolboxes provided by nature, to which food technologists have added 'artificial' colloids, e.g., gas bubbles, oil droplets, ice crystals, fat crystals, and protein aggregates, created by external forces (e.g., extrusion, compression, electric fields) or heating applied by food processing equipment (R. Van der Sman & Van der Goot, 2009). With these 'artificial' colloids, foods adhere to the length scales dictated by our tasting senses, which are sensitive enough to detect structures of millimetre down to micrometre size (R. Van der Sman & Van der Goot, 2009). In this sense, a palatable food must be designed by finely modulating these structures to enhance their nutritional function as well.

The structure of all foods can be imagined as the result of combinations of structural elements provided by nature or imparted during processing and preparation. Food structure design is the dedicated conception and fabrication of foods in such a way as to attain specific structures, functions or properties (Guo, et al., 2017). Knowledge on how foods and beverages interact with the digestive system, where they transform into supramolecular structures, can in fact have a direct impact on the rational design of such advanced materials for functional food delivery applications. For example, delivering a complete diet with a content of hydrophobic, amphiphilic, and hydrophilic nutrients, which is personalized to the needs of the consumers, could be beneficial for clinical and infant nutrition (Salentinig, 2019). Otherwise as confirmed by recent studies on the use in pasta formulation of alternative flour from different sources, such as potato and pigeon pea flour (Sharma, Dar, Sharma, & Singh, 2021) or flours from legumes such as chickpea (El-Sohaimy, Brennan, Darwish, & Brennan, 2020; Garcia-Valle, Bello-Pérez, Agama-Acevedo, & Alvarez-Ramirez, 2021) or bean (Romero & Zhang, 2019), pasta nutritional profile is usually improved, leading to an increase in protein, ash, fibre

contents, and antioxidant compounds together with a decrease in the starch content and of *in vitro* starch digestibility. What is missing in these approaches, solely accounting for the nutritional profile, based on the composition of the ingredients, is the input related to the target structural characteristics at different scale lengths. Although structure has been shown to have an equally important impact on nutritional quality, a novel food is designed with great care for its composition, stability and acceptability but, often, its structural optimization for nutrient accessibility is omitted in the preliminary conceptualisation phase and studied only *ex post*.
Ultimately, the food structure design has the potential to be personalized to digestive conditions and dietary nutrient requirements of the consumer or patient. From a nutritional perspective, the ability to control food digestion is extremely important to design food with desired characteristics: the key to control such process is to modulate the accessibility of digestive enzymes to their substrate. Recently, considerable interest has also arisen in the application of by-products of food processing with specific properties in food structure design, such as agar or locust bean gum substitutes.

6. Predictive models for designing the optimal structures: choice of parameters for artificial intelligence

As described in the previous section, stability, palatability, bioaccessibility and bioavailability of nutrients are the target properties of food optimization. These properties must be expressed using numerical descriptors, such as concentrations of degradation biomarkers, food sensory scores, preferably assessed by instrumental devices (electronic nose or tongue), post-prandial nutrients level in blood. Chemical and instrumental sensory analyses provide objective parameters intrinsic to the food, that are independent from the individual interaction with it. Conversely, parameters related to the digestive functions are strongly linked to the subjects' variability. For this reason, experiments simulating different individual physiological and pathological conditions are necessary, even when characterizing the target properties of a single food. Whereas *in vivo* experiments give a global indication of food nutrients digestibility in its full biological context, and *in vitro* experiments provide more insight into the different chemical and physical mechanisms, the mathematical, or *in silico* modelling can connect these two domains (E. Capuano & A. E. M. Janssen, 2021). The hydrolysis kinetics of the main macronutrients (proteins, starch, and lipids) are modelled to predict the concentration and their degree of hydrolysis in one or more compartments of the digestive system, or to predict the transport of the food through the digestive system. The most popular approaches assume the digestive tract as a series of bioreactors that can be described by mass balances, written as a set

of differential equations (Gim-Krumm, Donoso, Zuñiga, Estay, & Troncoso, 2018; Somaratne, et al., 2020). In recent years, models that also consider the food matrix together with the reaction and diffusion phenomena have been developed. Modelling of the swelling of protein gels by using the Flory-Rehner theory has been combined with the Gibbs-Donnan theory to include the distribution of ions between the gastric juice and the protein matrix to gain a better understanding of the phenomena that are essential in the digestion of the food matrix (R. G. M. van der Sman, Houlder, Cornet, & Janssen, 2020). Up to now, the role of modelling has been that of linking and explaining in vivo and in vitro experiments. However, a further step is required to use modelling for food properties prediction as a function of food structure. Suitable numerical descriptors of structure are required as inputs for AI systems, to predict properties that can define food in a functional way.

In the next section, available emerging approaches and those foreseen for the next future are described, emphasizing how structure descriptors have been employed to predict sensory properties and stability toward chemical transformations.

6.1 Describing the structure with imaging

The most straightforward way one can think of to parametrize food structure is through descriptors extracted from imaging. Given the number of existing imaging techniques (microscopy, spectral and hyperspectral imaging, nuclear magnetic resonance imaging, ultrasound, microwave, etc.), many different aspects of food structure can be characterized and digitalized. Furthermore, each imaging technique has its own array of analytics and descriptors, capable of grasping and describing physical quantities tied to the physical nature of the specific imaging technique. All these heterogeneous descriptors, together with general texture analysis and computer vision descriptors, that can be obtained from images under certain conditions, constitutes interesting inputs for artificial intelligence (machine and deep learning) frameworks. As a matter of fact, the role of artificial intelligence in describing food structure from images, is that of finding complex relationships between heterogeneous features describing different aspects of the structure and the different structure-dependent properties of a food. Furthermore, researcher in the field of deep learning, will rightfully argue that in the next future, a general characterization of structure directly from images without a-priori features and descriptors knowledge or assumptions could be possible. From an operative point of view, this means feeding a neural network, as complex as needed, each pixel (or voxel in 3D) of an image as an input and let the network learn how to build the best features to describe the problem (in this case, predict food properties from structure description). To reach this goal, huge quantities of

suitable training data are however required to avoid some known problems of deep learning architectures, such as overparameterization and overfitting. While some imaging techniques are inherently suitable for the high-throughput standardized data production (such as magnetic resonance imaging) required by deep learning architectures to achieve good prediction and generalization, other imaging techniques (such as electronic microscopy) suffer from a series of issues that make them less suitable for automation and high-throughput data production. Overall, we are quite far from the data production required to have a huge amount of labelled training data, especially regarding certain imaging techniques. In the next section, a high-throughput imaging technique (MRI) and a high-resolution imaging technique (electronic microscopy) are compared in terms of descriptors and suitability for automation. This is done to outline possible directions to facilitate an efficient use of artificial intelligence at this stage of structure description.

6.2 On the suitability of data production and imaging parameters for AI: a comparison

To grasp the meaning of what has been said in the previous section about data production and generality of descriptors, it may be useful to focus on a comparison between electronic microscopy (high-resolution, non-high-throughput) and magnetic resonance imaging (low resolution, high-throughput). Table 2 sums up the main categories of descriptors that can be extracted from images coming from these two different techniques, followed by a synopsis highlighting the upsides and downsides of each technique as far as automation and generalization are concerned. While MRI has many upsides when it comes to data production, generalization, automation of analysis and feature extraction for classification, a trade off exists in terms of spatial resolution. On the other hand, advocating the importance of high-resolution aspects in terms of food structure description implies the necessity of high-resolution imaging techniques. Electronic microscopy can fill in the role provided it becomes suitable for high-throughput data production and data-driven modelling. At present, microscopic image production is not optimized for automatic extraction of general features and descriptions, which are at the core of frameworks using integrated data and automated workflows based on machine learning. The first issue comes from image acquisitions inherently suffering from parameter dependency. Lighting conditions and magnification which are obviously related to experimental purposes, tend to shift microscopic imaging production toward less generalizable datasets. Moreover, most canonical morphological and structural descriptors that are quantified from this type of imaging, while being directly related to physical and easily interpreted quantities, require specific assumptions (i.e., presence/absence of pores, spheres, shapes, fibers

etc.). Characterizing portions of images with ad-hoc assumptions is ill-suited for automation and generalized parameter extraction. On the other hand, the power in terms of spatial resolution of electronic microscopy cannot be overlooked when trying to characterize food structure. The solution may lie in shifting microscopy data production toward a more pipeline-oriented way. The creation of a consensus for data harmonization of microscopic images in the field, could lead to parameter and feature extraction based upon low level and more general operators, analogous to the ones used for MR images. This shift of paradigm in data production and descriptor extraction, may contribute to boost modelling by facilitating the linking of the many levels of complexity characterizing real life foods, using general parameters. A shift in data production is also needed to pave the way for efficient deep learning approaches.

6.3 Structure images and sensory quality

Some scientific research, considered as an original reference works for these aspects, have laid the foundations for the way a set of fundamental or derived parameters X, defining the food structure, can be linked to a functional property Y through a mathematical function (Langton, et al., 1997). For instance, the microstructural parameters may be presented as the estimated model parameters A and B necessary to solve a correlating equation, e.g., $Y=A+B \log X$, where Y is a sensory vector descriptor, X the model matrix for microstructural parameter. The exemplary work by Langton et al. (1997), carried out on whey protein gels, defined nine quantified microstructural parameters constituting the X vector feeding the model: four parameters were the output of the digital image analysis (i.e., pore size at x20 magnitude; pore size at x40 magnitude; particle size; amount of threads), and five parameters were mode of aggregation as perceived by the test panel and already explained at the end of section 3 (Porosity; Clusters; Conglomerates; String of beads; Hairiness). Principal component analysis (PCA) of the textural sensory data identifies two groups: (i) grainy appearance, gritty, creamy and falling apart; and (ii) soft, springy, surface moisture and sticky. To find trends in groups of variables (microstructural and sensory variables), PCA on the whole data set was performed. The PCA had the purpose of creating, for each orthogonal component, linear combinations of variables characterized by a high degree of co-variance, thus evidencing their interdependence, by collecting them in different groups. One group of variables, defined by the large and small star volume of pores, the star volume of particles, porosity, clusters, gritty, falling apart and creamy (and acid) was found to take part in the systematic variation. Two groups of microstructural parameters and sensory descriptors were found: one group depending on the

dimensions of the overall network and the other depending on the shape of the strands and filling of the pores. This kind of data analysis made the model building a realizable approach.

6.4 Structure images, water dynamics and chemical transformations

Food systems behaviour is strongly dependent on water. Besides water content in a food material, it is important to understand the water state and dynamics for a proper comprehension of properties and stability of food structure. Understanding changes in location and mobility of water represents a significant step in food stability knowledge, since water "availability" within the matrix profoundly influences the chemical, physical and microbiological quality of foods. Water mobility/dynamics can be described as a manifestation how "freely" water molecules can participate in reactions or how easily water molecules diffuse to participate in reactions occurring in different sites (Fundo, Quintas, & Silva, 2015).

Nuclear magnetic resonance is a powerful technique to investigate water dynamics and physical structures of foods, through analysis of nuclear magnetisation relaxation times, because it provides information on molecular dynamics of different components in dense complex systems. The application of this technique may be very useful in predicting food systems physicochemical changes, namely texture, viscosity or water migration (Fundo, et al., 2015). Finding correlations amongst parameters based on time domain (TD)-NMR T2 decays, describing water dynamics, and texture-derived features based on SEM images is a challenging issue, when the aim is the quantitative characterization and parametrization of porous food matrices and the transformation that food undergoes due to processing (such as cooking). A comprehensive pipeline for parameter extraction, describing the porous food at different cooking time, must be set accurately. TD-NMR raw data are preferable to classical exponential fitting parameters, for building a general model accounting for the water status, as different phenomena participate in the modulation of the relaxation times of the water population in the compartmentalized porous matrix. For this reason, when matrix effects are investigated with TD-NMR, a probabilistic PCA with Radial Base Function (RBF) kernel may constitute the solution to find a latent space explaining differences in data tied to different matrices (pasta type) and cooking times. The RBF kernel can take the non-linearity of decays into account, projecting data into a suitable latent space, as shown in section 8.

The next section outlines the necessity to take another level of complexity into account when trying to predict bioavailability and bioaccessibility: the physiological interaction with the human organism.

7. Digital twin of a food must include its structure

Recently, a standardized food model (SFM) representing a typical US diet has been developed to facilitate these investigations. This model consists of caseinate-stabilized fat droplets, free casein, pectin, starch, sucrose, and sodium chloride. The SFM was stable to creaming for 2 days, contained small particles ($d \approx 180$ nm), and had a narrow particle size distribution (Zhang, Zhang, & McClements, 2019). It would, therefore, be beneficial to have an SFM with a harmonized composition and structure that could be used by researchers in different laboratories to test food matrix effects. This model would allow researchers to obtain reproducible results under standardized conditions, thereby leading to an improved systematic understanding of the influence of the food matrix on oral bioavailability of different bioactive agents. It may then be possible to establish general trends between bioactive type and the magnitude of food matrix effects (Zhang, et al., 2019). However, gathering an almost infinite set of model foods covering each possible category is a difficult, if not impossible, goal to achieve. For this reason, having an exemplary set of model foods available, the next step could be to create *in silico* models, derived from the mathematical combination of the basic models, to simulate each existing real food. In other words, starting from physical model foods, virtual simulator of foods can be generated.

As previously stressed, *in silico* simulations of food as complex particle based soft matter, are strictly bound to the various length scales in the structure and occurring phenomena. As such, different properties must be simultaneously investigated at different scales, from mesoscale to nanoscale. While mesoscale properties (i.e. for emulsions and fat droplets) can be investigated using coarse-grained particle-based simulations (Morris & Groves, 2013), at finer length scales quantum-mechanical effects might occur. While hybrid multiscale models, capable of joining coarse and fine level descriptions, are already available (Bolnykh, et al., 2019), making predictive multiscale simulation approaches seemingly viable, the true complexity of food as a system is still unaddressed. A complete review of available simulation tools, with a breakdown of all the levels of complexity that must be addressed while trying to predict food properties and functionalities from its structure and molecular-level interactions, is provided by Barroso da Silva, et al. (2020). Amongst other issues, a predictive model relying solely upon multiscale simulation, can suffer from high computational complexity. Simulating systems consisting of extremely high number of particles, for which free-energy properties and kinetic properties must be computed for several time-steps, can easily lead to unrealistic computational time, even for specialized high-end hardware. However, machine and deep learning can prove useful in decoupling multiscale descriptions from approaches based exclusively on simulation.

Quantitative structure-activity relationship (QSAR) based approaches are, in example, very useful in predicting bio-chemical properties of compounds, including biological activity (Neves, et al., 2018). These approaches are based on linking sets of molecular descriptors to a given response variable; essentially the goal is to find a solution to a supervised learning problem by coming up with an optimal set of user-defined molecular descriptors and a suitable model to link them to the outcomes (response variable). A recent development of such a framework involves the use of deep learning architectures, using recurrent and convolutional neural networks (Chakravarti & Alla, 2019). The use of such neural networks allows for a generalization of the learning problem, by eliminating the necessity of an a priori definition of the molecular descriptors, at the cost of a very high pool of training data. Approaches of these types, when the interpretability of the network-extracted descriptors is ensured, can minimize the bias introduced by the users when choosing the descriptors and the difficulty of interpreting descriptors that are not directly related to chemical structures. Results from these types of framework, can furthermore be linked with outcomes from physiological experiments (i.e., experiments involving digestibility or involving health effects of certain compounds). In this way, the molecular scale and the macroscale of physiological effects are encased in a multiscale data-driven description. In a similar and more general fashion, many levels and scales of complexity can be linked through machine and deep learning, by finding ways of extracting general descriptors to be related to a response variable. Given the sheer complexity of food, data-driven description of the various levels of complexity of food structure and food-human interactions seems to be a promising way of predicting properties and health effects.

In the next section, an example of how to extract joint general descriptors from different scales of complexity (water-matrix interaction and morphology) of a real-life food, that can be ultimately related to outcomes from physiological experiments, is presented.

The example, set up by the authors, shows how to use SEM images in a more general way, by extracting texture analysis descriptors, when the acquisition experimental design is suitable. An example of how to correlate such structure descriptors to properties such as water mobility, using raw data and machine learning, is also proposed.

8. A case study: spaghetti pasta

8.1 Designing food structure for food shaping

The structure is responsible for the sensorial, textural and nutritional properties of pasta, and its formation relates to the characteristics of the raw ingredients and to several unit operations of the manufacturing process (Scanlon, Edwards, & Dexter, 2005). In particular pasta structure

and quality depend on gluten and starch properties (Desai, Brennan, & Brennan, 2018; Witczak & Gałkowska, 2021) and on their physical-chemical modifications (protein denaturation, starch gelatinization and swelling, etc.), occurring during pasta production process as well as the time of cooking. Traditionally, dried spaghetti pasta is produced by mixing durum wheat (*Triticum turgidum, subsp. Durum*) semolina and water (generally ~30 g /100 g), followed by a series of unit operations such as extrusion, drying and packaging. The appropriate selection of ingredients and technological parameters is fundamental, since it directly influences pasta quality and structural features but, in turn, also affect content, digestibility and ultimately the bioavailability of macro-nutrients (starch, proteins) and micro-nutrients (minerals, phytochemicals). Since customers currently prefer pasta with uniform amber colour, firm texture ("al dente") and shape retention when cooked, it is of commercial importance to analyse the cooking characteristics of pasta to design and develop a high-quality pasta that satisfy consumer demands. Furthermore the increasing demand for innovative pasta products is encouraging research on novel raw and processed materials such as dietary fibres, legume flours, rice, corn, emmer, cricket flour - to meet the consumer demand in terms of nutritional, sensory and technological value of pasta (Romano, Ferranti, Gallo, & Masi, 2021). In this regard, cooking properties such as texture parameters (e.g. firmness and elasticity and shape retention), cooking time, cooking loss, water absorption index, swelling index (Ficco, et al., 2016; Susanna & Prabhasankar, 2013) are very important indicators of pasta quality. The texture of pasta is the most important consumer attribute of pasta that influences consumer acceptance (Susanna & Prabhasankar, 2013). In particular, firmness can be related to protein content as well as the starch composition and it is a reflection of the bond strength and the integrity of the protein matrix present in the pasta after the cooking process (Dexter & Matsuo, 1979). Microstructural changes of starch and proteins during cooking depend on water availability, and the kinetics of solvation of each biopolymer have a major role on the final texture of cooked pasta (Bonomi, et al., 2012).In order to control the cooking quality of pasta, it is necessary to understand structural changes during the boiling process that affect textural and sensorial properties of pasta. Primarily made up of carbohydrates (70 g /100 g) and proteins (11.5 g / 100 g), cooked pasta is ingested as a solid food with a compact and "al dente" texture and requires a low degree of mastication before swallowing, after which the pasta arrives in the stomach in the form of large solid particles. It is considered to be a slowly digestible starchy food with a low or medium Glycaemic Index (GI) (Gallo, Romano, & Masi, 2020; Granfeldt & Björck, 1991). Generally, a compact and dense microstructure is attributed to the pasta, which: i) limits water absorption and thus starch swelling and gelatinization, during cooking; ii) entraps

the starch granules reducing the accessibility of α-amylase (Jenkins, et al., 1983) and (iii) releases α-amylase inhibitors during cooking that can immobilize the enzyme into the gluten network (Zou, et al., 2019; Zou, Sissons, Gidley, Gilbert, & Warren, 2015). The major challenges for pasta industry are now to increase food healthiness and customized nutrition content and compositions but keeping high sensory attributes and technological performances. Multiphysics simulations approaches could improve the efficiency of certain food manufacturing processes and facilitate the sustainable packaging of food, for instance, by creating morphing pasta that can be flat-packed, to reduce the air space in the packaging. It is possible to induce temporary asynchronous swelling or deswelling that can transform flat objects into designed, three-dimensional shapes (Tao, et al., 2021). How does it work with a different microstructure associated to a functional pasta? Does the pasta morphing affect the water-matrix interaction upon cooking?

8.2 Cooking and water-matrix interaction

To date, the structure of cooked pasta has been analysed at various microscopic and mesoscopic levels by means of different methods, such as MRI. In fact it can be used to evaluate water distribution and mobility in dry pasta, and in pasta at various cooking time (Bernin, et al., 2014). Even these studies revealed that water penetration, distribution, and mobility during cooking were highly dependent on the degree of protein reticulation, which in turns is greatly affected by process conditions and food formulation (Tao, et al., 2021) MRI represents a non-invasive method that spatially resolves the amount and dynamics of water and macromolecules-protons. For this reason, Bernin, et al. (2014) used MRI to make a real time assessment of the effect of starch-gluten ratio on water distribution in dry spaghetti during cooking. Therefore, investigating such properties can help to understand how pasta components (water, gluten, starch, fibre, etc.) interact with each other defining its structure, quality, acceptability, and stability. In this respect, Gallo, et al. (2020) investigated the impact of pasta composition (semolina and durum whole-wheat semolina) on water mobility in spaghetti before and after cooking by low-resolution 1H NMR experiments. In detail T1 and T2 proton relaxation times as indicators of the molecular water mobility, have been determined (Gonçalves & Cardarelli, 2019). The uncooked spaghetti had T1 and T2 values much lower than the cooked ones suggesting a very low water mobility in the dry pasta. With increasing cooking time, it was observed a significant increase of both T1 and T2 relaxation times, either for semolina or whole wheat spaghetti, suggesting that molecular water mobility within the pasta structure increases as protein coagulation and starch gelatinization proceed (Gallo, et al., 2020). According to

Bosmans, Lagrain, Ooms, Fierens, and Delcour (2013), this behaviour could be explained in term of three phenomena: i) water uptake in pasta structure; ii) starch gelatinization with the subsequent destruction of the original structure; iii) gluten polymerization accompanied by water expulsion from the gluten network. By comparing the behaviour of the two samples, one observes that the presence of fibre led to a reduction in water mobility, since they can keep a substantial excess of water during the cooking process (Serial, et al., 2016). The intermediate zone was characterized by swollen starch granules embedded in a coagulated but dense protein network; the presence of fibre resulted in an irregular structure in which there were a small number of still intact and therefore non-gelatinized starch granules. As reported by Manthey and Schorno (2002), in whole-wheat pasta bran particles cause a dilution of the gluten proteins, interfering with proper gluten development. This results in a highly porous structure in which starch granules are more accessible to water molecules. Starch granules in the surface region were fully gelatinized and thus completely disintegrated in amylose and amylopectin. In the intermediate zone, starch granules were highly hydrated increasing in size

Concerning the analysis of surface roughness, laser microscopy stressed an irregular surface structure for dry pasta (due to the presence of intact starch granules) which became more homogeneous after 1 min of cooking, due to the starch gelatinization.

8.3 Toward the automatization of water-matrix interactions and structure characterization

Joining measurement of NMR T1 and T2 proton relaxation time with SEM images, seems a promising way of intertwining water mobility related phenomena with morphological variations, thus including structure into food characterization. Parameters extracted with these techniques, can furthermore be modelled using machine and deep learning architectures. However, both methodologies require a fair amount of expertise in acquisition and processing of the data, making standardization and automation of modelling pipelines challenging. Extracting parameters and quantities from SEM images, is especially challenging as it requires the use of dedicated software (e.g., when measuring particle size) to extract the distributions of nanostructures and microstructures in an image. Accurate particle size distributions can be difficult to obtain, as they require images with highly detectable particles and morphologies to build a suitable statistic. Furthermore, the observable size of particles and structures depends drastically on the viewing angle, while measures such as porosity and surface roughness are affected by lighting and zooming. A complete list of issues and standardization of measures for

SEM image analysis is provided by the ISO (International Organization for Standardization)[1]. On the other hand, NMR relaxometry, while being a high-throughput technique with relatively low acquisition times and high reproducibility, requires expertise in sample preparation and acquisition sequence engineering. Furthermore, studying T1 and T2 distributions with inversion software such as the UPEN algorithm[2] requires a deep understanding of the physical and mathematical nature of the inversion problem, making this kind of analyses extremely variable and elaboration parameters dependent.

8.4 Is learning from raw data and general descriptors promising?

A possible way to bypass some of these issues and make automatization and learning easier, moving toward a more general framework, is to analyse raw TD-NMR decays and study SEM images by extracting general texture analysis features and learning latent components in the data, instead of specific measurements and physical quantities. In this qualitative example, a way to correlate water mobility phenomena and morphology related features using machine learning is proposed. SEM images of different zones of semola spaghetti, acquired at different cooking time points, are processed and segmented using various filtering techniques and morphological operators. A set of minimum image acquisition parameter can be chosen (i.e., zoom, lighting, well defined morphological regions of the pasta to acquire), to minimize variability in the final dataset related to possible acquisition biases.

The 13 Haralick descriptors (Haralick, Shanmugam, & Dinstein, 1973) are computed from the images of the complete cooking profile of the pasta. These general descriptors, widely used in texture analysis and computer vision, are moments computed from the segmented image cooccurrence matrix. These moments are intended to describe the characteristics of the patterns of the textures of the image, in term of the probability of occurrence of grey levels. As such, they serve as general morphological descriptors, whose relationships with descriptors extracted from TD-NMR can be estimated. These descriptors can be studied as a function of time-dependent latent components extracted from TD-NMR raw decays, with a process summarized in Figure 2, to find links with water mobility related phenomena.

As an example, typical raw decays of pasta at different cooking time points, are shown as projection into a latent variable space using a probabilistic KPCA (Kernel Principal Component Analysis). Using an RBF kernel in a self-optimizing learning pipeline, each decay curve is

[1] https://www.iso.org/obp/ui/fr/#iso:std:iso:19749:ed-1:v1:en

[2] https://iopscience.iop.org/article/10.1088/1361-6420/33/1/015003

projected into a lower dimensional space with the aim of detecting differences tied to phenomena occurring during cooking (Figure 3a). Some of the Haralick descriptors appear to have strong linear and non- linear correlations with the time dependent latent variables extracted from TD-NMR raw decays (Figure 3b). Moreover, correlations seem to be different from zone to zone, highlighting the expected behaviour of TD-NMR to discriminate information about different characteristics of water populations at different cooking times in different pasta zones. Some texture analysis descriptors, such as texture Sum Average (HF6, y axis of Figure 3b) which is tied to "homogeneity" of the texture, describing the central zone images, show an exclusively monotonous relationship with cooking time and PC scores (both PC0 and PC1) after a certain cooking time (Morphologic Phase, Figure 3b). Looking at the KPC space, this phenomenon corresponds to a steep variation in PC1 score and a low variation in PC0 scores. On the contrary, below this time (orange to yellow points, Figure 3a), steep variations along PC0 and slow variations of PC1 scores are encountered, until PC1 score variation minimum is reached (red points, Figure 3a). After this, variation on PC1 scores starts to rise again (Activation, Figure 3b) while PC0 scores variation starts to reach its minimum. Above this threshold of cooking time, both PC1 and many HF descriptors, such as HF6 in Figure 3b, start a trend with a strict monotonous dependence with time. This time point may represent the threshold for which changes in the texture of the matrix start to be exclusively dependent on cooking time, maybe due to the irreversible rupture of structures in the food matrix and the consequent variation of the timescale of water exchanges. Looking at Figure 3, one can argue that the description of the morphological changes emerging from these preliminary results, is in agreement with findings from Manthey and Schorno (2002). If in the early moments of cooking starch gelatinization prevails, the resulting SEM images tend to show more homogeneous surfaces, with little differences from a morphological point of view. However, with raising cooking time the observed increase in the inhomogeneity of pasta surface and the changes in water mobility become a monotonous function of cooking time, as the partial detachment of solid materials such as starch and starch-attached proteins probably becomes the prevalent phenomena. Haralick descriptors for SEM images, together with self-learned latent components extracted from TD-NMR raw decays, are capable of picking up this sort of threshold behaviour and successfully merging description of the morphology and water-matrix interaction. Learning latent features and parameters from raw NMR data and images processed to a bare minimum, studying and understanding the correlation amongst the extracted descriptors can help building digital twins of food with an included structural characterization of the matrix. In the example, water mobility and morphology are investigated with a general

data-driven framework, using machine learning and canonical texture analysis to find suitable features and descriptors. The main advantages of this approach are the generality and the lack of assumptions needed for the description of structural elements from images. Using raw data (such as T2 decays in the example) and letting AI methods learn the best way to represent them is optimal when dealing with many heterogeneous datasets, in terms of automation and feature discovery. Moreover, bypassing the necessity of assumptions when describing structure from images, becomes an advantage when parametrizing real-life foods in which matrix structures can be extremely heterogenous along the different length scales. Consequently, different types of images and raw data from experiments regarding digestibility, stability and bioaccessibility can be explored to shed light on their relationship with structural properties, even with complex real-life food.

9. Conclusions

Understanding how formulations of ingredients and unitary operations of food processes make up the structure of food and how this structure changes during its shelf - life or eating will play an important role in the development and management of food science and industry. Much of the information that defines the structure of a food is currently neglected when entering the domain of nutrition, as the structural dimension is too complicated to be quantitatively measured and related to sensorial properties, stability, digestibility and bioaccessibility of nutrients. Not even the momentum given by the considerable progress achieved in the design of functional foods has so far been sufficient to assign the correct importance to the structural nature of food. Certainly, the complexity of the information is such as to hinder the creation of predictive-based models based on analysis of a limited amount of available data. For this reason, it is certainly conceivable a considerable impulse determined using artificial intelligence capable of handling certain quantities of heterogeneous data. It would be useful to be able to predict the sensory quality and stability of food designed to become carriers of healthy nutrients through images that shoot their supramolecular structure. It would be also desirable for these same foods designed *in silico*, to predict the duration as a function of the dynamic state of the water capable of modulating the chemical transformations underlying physiological or anomalous phenomena, also to include the aspect of sustainability in the conception phase. A model food such as pasta, widely consumed all over the world, object of studies for possible functionalization as a vehicle for bioactive substances useful for health, can serve as a case study to build a pipeline of an automated approach. The endpoint of such a pipeline is a direct extraction of information on rheological and sensory properties starting from images of the

structure and from raw data of the dynamic state of the water. The main advantages of such a framework are: i) an efficient automatization of parameter extraction useful for building suitable inputs for AI architectures, which require high-throughput data for proper training ii) a more efficient and general way of extracting parameters especially from imaging; using general parameters for image analysis instead of measured technique-dependent parameters or measured quantities that requires ad-hoc assumptions on structures (i.e. presence/absence of pores, fibres etc.), can prove more useful given the high heterogeneity of structural elements at different length scales iii) a more efficient way of linking different levels of complexity of structure description and properties to be predicted, through the use of general parameters and features learned directly from data with machine learning; this step is crucial to avoid oversimplification generated by canonical interpretative models. However, extending this framework to all the aspects of food modelling for properties prediction, poses quite a few challenges. The first one is a required shift of paradigm of imaging data production. Certain techniques (such as SEM) suffer from a lack of a consensus of acquisition standards, hindering data harmonization which is essential for high-throughput input production. Another major challenge is the complexity of modelling and parametrizing properties such as bioaccessibility and bioavailability. These properties not only require a comprehensive parametrization of the structure to be predicted but are also linked to the interaction with digestive functions. The interaction with the human organism, especially with GIT functions, adds a whole new level of complexity that must be addressed. The compartments of the GIT and their functions are interlinked and impacted by food structure, while also being subjected to interindividual variability. Hybrid approaches linking structure at molecular level and physiological outcomes, based on deep learning architectures, are however gaining popularity (section 7) due to their computational performances.

The ultimate goal of AI oriented frameworks is to be able to make more limited use of expensive and time-consuming experiments on physically prepared foods, by using digital twins of foods designed in the laboratory. This, in turn, could lead to a more efficient data production for studies of physiological outcomes of functional foods.

Further advances for future applications of AI in food science and technology may arise, as in medical sciences, from the enormous expanse of data resulting from the exploitation of different types of heterogeneous information (images, chemical analysis results, physical measurements, etc.) in the same system, for example a single neural network, integrating food data from different scales and sources. The challenge, in this case, is to give the right importance to one type of information over the others.

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Caption to Figures

Figure 1. *Food matrix is defined by structures at different length scales consisting of elements spanning nanometres to millimetres and above. Many of the important properties of foods are determined by structural elements at microscale. Molecules such as carbohydrates, proteins, and lipids, indeed form supramolecular clusters that behave as pseudo-molecules of higher molecular weight. Linking organised structural elements to food properties through imaging may be feasible by means of artificial intelligence applications.*

Figure 2. *The process behind the decomposition of T2 decays raw data into a lower dimensional space. Each time point of each decay is interpreted as variable and fed to a probabilistic PCA with an RBF kernel. Data are transformed according to coefficients which are dependent on the kernel parameters, optimized through machine learning. An example of resulting latent space is showed in the following Figure 3a, where each T2 decay, measured for each different cooking time, is represented as a point in a two-dimensional space.*

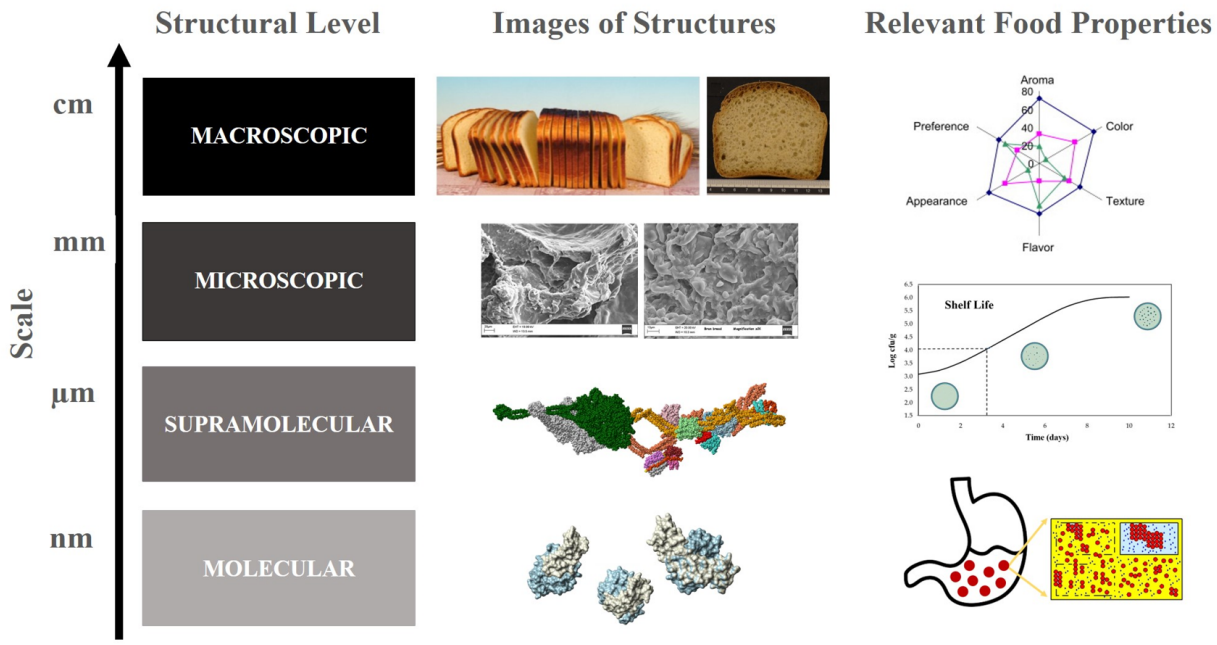
Figure 3. a) *Resulting lower dimensional latent space, computed according to Figure 2. In this space, each T2 decay measured at different cooking times (indicated by the colour gradient) is represented as a point. The points are the projection in the 2-d latent features space, learned by the kernel, of each T2 decay. In this space, differences tied to effects of cooking on water mobility are the most detectable.* ***b)*** *Scatter plot of PC0 vs HF6 (Sum Average, computed from SEM images of the central zones). A qualitative interpretation of the relationship between these two variables can be given as follows: in the functionality phase, water mobility is mainly related with starch gelatinization phenomena, resulting in little morphological changes. After an activation phase, where the rupture of structures in the food matrix begin to arise, the morphological changes detected in images start a strictly monotonous trend related to cooking time (morphology phase).*

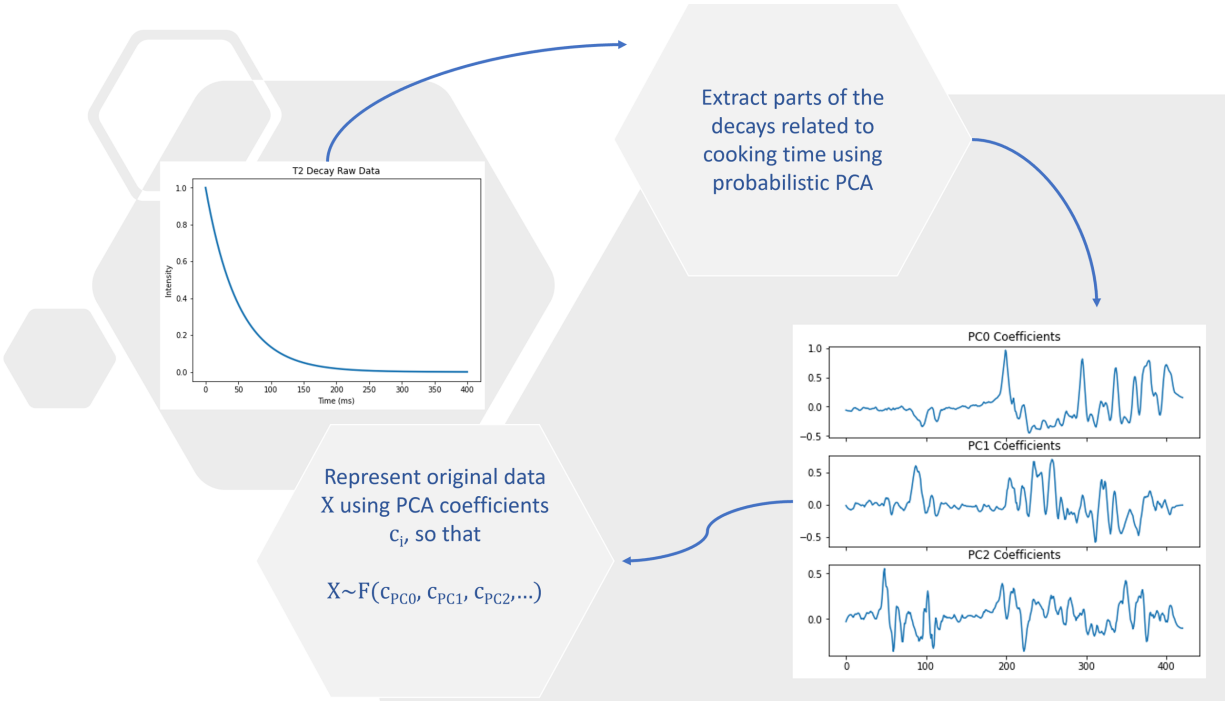
Table 1. Principal methods for structural analyses at characteristic length scales in foods, appearance of food matrix and structural elements

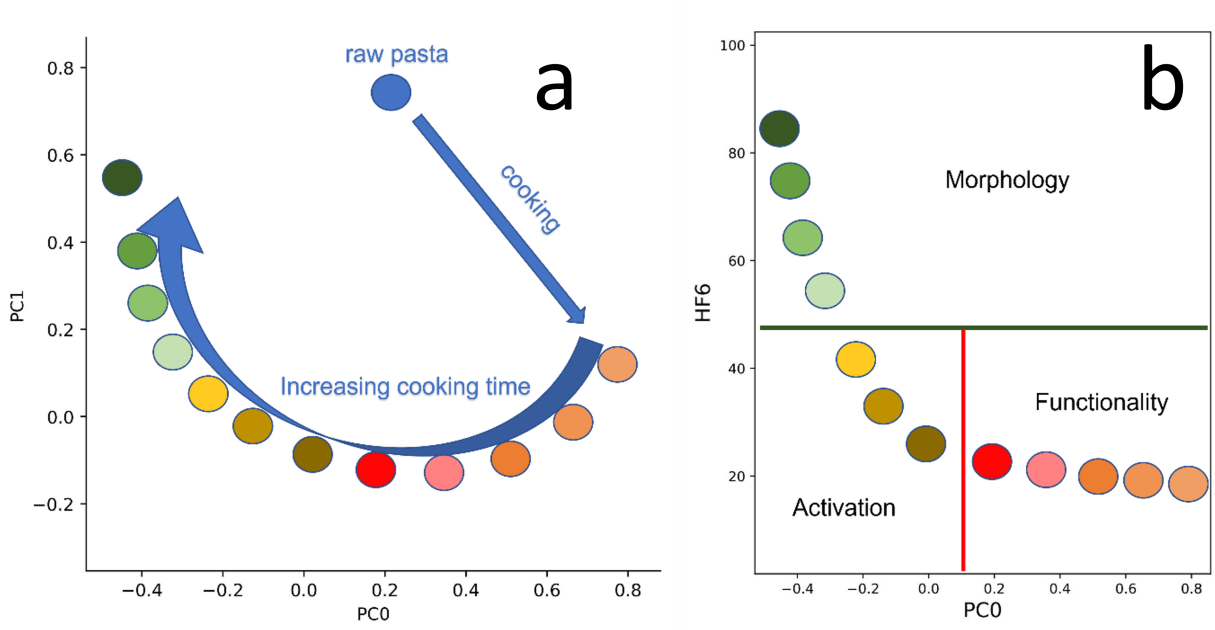
SCALE LENGTH	METHODS	PHYSICAL STATE / STRUCTURAL ELEMENTS	INFORMATION ON:
> 1 cm	• Texture analysis • Image analysis • Sensory panel	liquid, gel, solid, porous solid	-properties of network at large deformation - size and shape macrostructural elements -sensorial attributes (e.g., appearance, colour, firmness, overall acceptability)
1 mm – 1 cm	• Texture analysis • Microscopy	liquid -aqueous matrix (*aqueous phase in fruit juices*), liquid -emulsion matrix (*mayonnaise*), gels (*desserts, processed meats*), porous matrix (*bread, extruded snacks*), viscoelastic matrix (*dough*), etc.	-properties of network at large deformation related to eating properties -microstructure
1 - 500µm	• Confocal microscopy • Light microscopy • Rheology	micelles (*casein micelles*), droplets, air cells (*bread bubbles*), crystals (*salt*), fibres, granules (*starch granules*), etc.	-size and shape of structures -properties of network at small deformation -ingredient interaction
10 -500 nm	• Light scattering • Electron microscopy	micelles (*casein micelles*), droplets, air cells (*bread bubbles*), crystals (*salt*), fibres, granules (*starch granules*), etc.	-aggregation, density, arrangement -size of structures
< 10nm	• Raman • Chromatography • Thermal analysis • SDS Page • NIR	carbohydrates (*starch*), proteins (*gluten, caseins*), lipids, water, etc.	-molecular structure -proportion of elementary parts -unfolding vs. native -denaturation /transition temperature

Table 2. Main descriptors and (dis)advantages for electronic microscopy and magnetic resonance imaging

	SEM	**MRI**
Descriptors	• Particle size and morphology • Pore size and morphology • Size distribution and morphology • Shape orientation (e.g., fibres) and diameter distribution (e.g., beads)	• First order grey level statistics (e.g., Histogram of grey levels statistics, symmetry of grey levels centred about the mean, entropy of the image) • Roughness of textures • Degree of linearity • Co-occurrence matrix statistics (e.g., Haralick moments) • Structural or morphological features of ROIs (e.g., Bounding ellipsoid volume ratios) • Transform features (features extracted in frequency domains)
Pros & Cons	• Not immediately suitable for high-throughput production (parameter dependent acquisitions: lighting, magnification etc.) • No data harmonization standard due to heterogeneous necessities of application fields and experiments • Widely applied in many fields • Canonical descriptors immediately linkable with physical quantities • Very high resolution • Requires specific assumptions for image analysis (i.e., presence/absence of certain geometrical structures, pores, shapes etc.)	• Inherently suitable for high-throughput data production • Data harmonization standards are widely supported in many biomedical fields (neuro imaging, imaging for oncology) • Descriptors comes from low-level, general texture analysis and morphological studies alike • Low resolution • Does not require specific assumptions for image analysis, due to canonical analysis based upon general first order statistics of grey levels and moments of cooccurrence matrix.


Structural Level
Images of Structures
Relevant Food Properties
Scale
cm
mm
µm
nm
MACROSCOPIC
MICROSCOPIC
SUPRAMOLECULAR
MOLECULAR
Aroma
Color
Texture
Flavor
Appearance
Preference
Shelf Life
Time (days)


T2 Decay Raw Data
Intensity
Time (ms)
Extract parts of the decays related to cooking time using probabilistic PCA
PC0 Coefficients
PC1 Coefficients
PC2 Coefficients
Represent original data X using PCA coefficients c_i, so that
$X \sim F(c_{PC0}, c_{PC1}, c_{PC2}, \ldots)$


a
raw pasta
cooking
Increasing cooking time
PC1
PC0
b
Morphology
Functionality
Activation
HF6
PC0

- Supramolecular structure is important for in-silico design of functional foods
- Models based on artificial intelligence may predict optimal food structures
- Water-matrix interactions and structure must be included in digital twin of food