Chapter 1

Food Structure for Nutrition

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1.1 Introduction

The great tradition of nutrition research has seen the creation of an unprecedented knowledge base of the essential nutrients, together with their absolute quantitative requirements at different life stages, and the pathological phenotypes experienced by populations who fail to consume sufficient quantities of them. The research that was necessary to assemble this knowledge base of essential molecules is one of the life science's great achievements. In retrospect, the achievement was made possible by some key strategic decisions by nutrition scientists. First, there was the critical decision for nutrition to become a molecular science. The object of the study of nutrition, namely food, was physically and conceptually disassembled into individual molecules. By eliminating food structure from nutrition research, it became possible to feed animals with purified diets in which specific suspected nutrients were explicitly included or assiduously removed. If the molecule was an essential nutrient, its elimination from a diet fed to a growing, reproducing animal model would produce overt deficiency symptoms. This so-called 'fault model' of nutrient discovery was critical to scientific studies designed to identify the essential nutrients. As a result of this very successful research strategy, all of the vitamins, minerals, amino acids, and fatty acids that are essential to the growth and reproduction of animals and humans are now known.

The knowledge of the nutrients that are necessary for humans shifted the public health emphasis to strategies designed to ensure that populations consume diets that achieve adequacy of all of the essential nutrients, and are thus sufficient to prevent deficiency diseases. An underlying assumption in this public health emphasis and focus on essential nutrients was that diets containing all of the essential nutrients in adequate amounts would largely eliminate diet-related diseases. But it has become disturbingly clear that it is possible to obtain all of the essential nutrients and still consume diets that are suboptimal for overall health. In fact, poorly balanced diets are now recognized to be one of the leading causes of metabolic diseases around the world.[1] Understanding how diet can produce such diseases is leading to a much more comprehensive understanding of the interactions between food components and health.

To understand food's broader role in nutrition, it will be necessary not only to go beyond essential nutrients, and to redesign nutritional models and experiments, but also to reconsider the meaning of 'health' itself. Health must be understood in terms of the wide diversity of normal metabolic states of humans. The recent epidemics in heart disease, obesity, diabetes, hypertension, and osteoporosis indicate that health can deteriorate in response to imbalanced diets almost as quickly as it can deteriorate in the absence of essential nutrients.[2] In particular, there is an immediate need to understand the role of diet and foods in managing food intake and in regulating whole body energy status. Most nutritional measures of essential nutrients and their status have been taken in the fasted condition to avoid confounding chronic status with acute food intake.[3] It is now becoming apparent[4] that variations in the dynamic or temporal responses to food components are also important to overall health. Nutrition research must, therefore, embrace the entire continuum of the fed state, leading to an understanding of how rapidly foods are digested, absorbed, and metabolized, and how these temporal and special events relate to overall health. With this perspective in mind, the influence of food structure on the dynamics of varying post-prandial metabolic states should be studied in mechanistic detail.

Food itself must also be understood comprehensively as multi-component, multi-phasic ensembles of biomaterials. Clearly, optimal diets are more than just the essential nutrients. Notably, several aspects of foods have emerged that were virtually ignored by nutritional research in the scientific pursuit of essential nutrients. Perhaps the most important omission was food structure itself. The science of food biomaterials must now deliver food structure as a fully controllable variable set to nutrition research. For nutrition researchers to understand the role of physical, colloidal, and macromolecular structure, these must be studied as independent variables in nutrition studies. Knowledge of food structure must, therefore, become highly predictive – not just descriptive.

1.2 Food Structure and Nutrition – Then and Now

1.2.1 The Past

The science of nutrition is the knowledge repository for the understanding of essential nutrients, their quantitative requirements, and the mechanisms behind their essentiality. Few achievements in science have been as complete, or as rapidly brought to public health practice, as the identification of nutrients essential for humans. The decision taken early in the 20th century to disassemble food commodities into molecules and study essentiality as a molecular phenomenon was the defining event in molecular nutrition, and few decisions in the history of science have been so successful. The concept of specific molecules as essential amines was initiated by Casimir Funk, who effectively spawned molecular nutrition with the isolation of vitamin B1 (thiamin) in 1912, as reviewed by Jukes;[5] and within 40 years the concept of essential nutrients was ostensibly complete.

This great legacy of discovery paved the way for the eradication of diseases caused by nutrient deficiencies. However, some of the important strategies of nutrient discovery are proving to be debilitating to the future growth of nutrition as a field. This is particularly true as nutrition emerges with the goal of guiding diets to improve overall health. For example, while disassembling foods into molecules enabled the differentiation of essential from nonessential nutrients, it left a prevailing assumption that food *per se* is immaterial to the provision of essentiality, and to health in general. Similarly, by establishing essential nutrients, the underlying assumption was that they were essential for *all* humans; thus, varying nutritional requirements within individuals among the population remained largely ignored. By defining bioavailability as the integration of the pharmacokinetic curve of an ingested nutrient in blood relative to the same nutrient when injected, the goal became a bioavailability of unity; hence, the foods themselves – in particular those with a degree of complexity of food matrices that may reduce bioavailability – were by definition deleterious. By defining an adequate diet as that producing adequate tissue levels of nutrients in the fasted condition, the relationship of the structure of foods and diet to the dynamics of the fed state has remained largely unstudied. Needless to say, if the dynamics of food and nutrient delivery remain unknown, they will continue to be unappreciated in terms of the value of food structure to its nutritive value.

1.2.2 The Present

The emergence of diseases of metabolic dysregulation associated with variations in diet is forcing scientists to refine the traditional views of nutrition. Diet affects health in more ways than simply through providing essential nutrients: it includes various aspects of chronic metabolic regulation. The science of nutrition has not yet built an understanding of this complexity. Furthermore, whereas recommendations for essential nutrients can be quite broad for the entire population, humans vary in their responses to diets as they affect metabolism, and the same diets fed to different individuals may develop quite distinctly different health consequences. Therefore, as the field of nutrition faces this new challenge of (re-)discovering the importance of food, nutrition scientists will also need to change their perspectives of health.

While food structure and nutrition have not been well studied, there are clear indications of the importance of the dynamics of food digestion to health from many aspects of ongoing scientific research. The most vivid is the variation in rate of absorption of the simple nutrient glucose. Although food structure has not been explicitly specified as an independent variable, for many years the rate of glucose delivery to blood has been included as an indicator of food as the

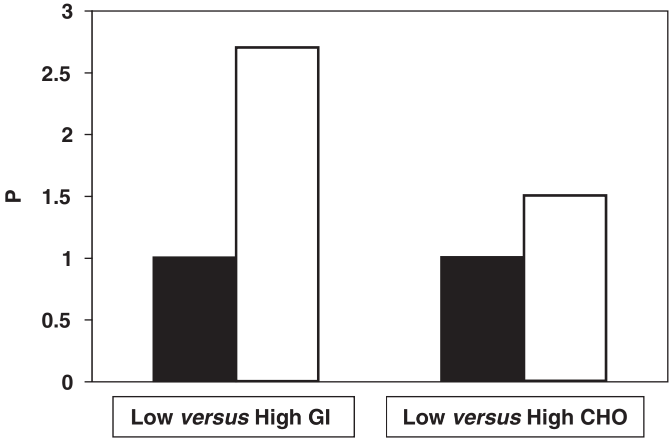

Figure 1 *Relative probability of developing premature macular degeneration (P) as affected by the glycemic index (GI) and the total carbohydrate (CHO) of reported habitual diets in the Nurses' Study population*[7]

glycemic index.[6] Numerous studies have documented the effect of glycemic index in accounting for variations in metabolic response to particular diets. Even more impressively, as glycemic index has been included as an independent variable in larger health issues, this simple surrogate reflection of food structure is being recognized as important to many end points that are not typically thought of as being related to food structure. For example, Taylor and co-workers[7] have shown that glycemic index as a dietary variable was associated with an almost threefold increase in risk of macular degeneration in the Nurses' Health Study population (Figure 1). Though many more studies have documented the effects on health of the rate of absorption of glucose as glycemic index, as reviewed by Dickinson and Brand-Miller,[8] little research has been pursued to extend these observations into a more precise understanding of the role of food structure in the dynamics of glucose delivery.

1.3 Food Structure and Bioavailability

Bioavailability is defined[9] as the difference in delivery to blood between an oral dose and an injected dose. It is determined experimentally by measuring the dose-corrected area under curve (AUC) of a substance administered orally (po) divided by the AUC intravenous (IV):

$$F = ([\mathrm{AUC}]_{\mathrm{po}} \times \mathrm{dose}_{\mathrm{IV}})/([\mathrm{AUC}]_{\mathrm{IV}} \times \mathrm{dose}_{\mathrm{po}}) \qquad (1)$$

If 100% of an ingested dose of a nutrient or a compound reaches the blood, the bioavailability (F) is considered to be 1. From the perspective of essential nutrients – especially when considering the risk of deficiency – the greater the bioavailability, the better the nutrient. Hence, food matrices promoting rapid and complete absorption were judged to be superior in their ability to deliver essential nutrients.[10] Food matrices that compromised rapid absorption, as a result of their structural complexity, were considered deleterious to bioavailability and hence to nutritional value. With these rather narrow but, in context, reasonable assumptions about food structure and nutrition, food processing steps that destroyed structure were advantageous and those that created structure were considered deleterious. Now that scientific considerations have begun to broaden beyond essential nutrients to nonessential food components and the food structure itself, the absolute dynamics of the delivery of food and food components is being studied. The key question then becomes: "what is the optimal situation – is it rapid complete absorption, or slow, perhaps even incomplete, absorption?" When such a question is asked, it becomes clear that there are no biological models of optimal food structure. This being the case, it is reasonable to ponder what is the preferable biological model one would wish to interrogate to answer questions about rate and extent of absorption of nonessential food components.

1.4 Models of Food Components, Food Structure, and Health

Nutrition has begun to address the scientific questions associated with nonessential food components in the diet. To date, most of these components have been derived from plants. The vast majority of small biological molecules as candidate bioactive food components are indeed derived from secondary metabolism in plants. The total number of secondary plant metabolites is estimated[11] to exceed 2×10^5. Nonetheless, in attempting to establish appropriate food components for nourishment beyond the essential nutrients, it is reasonable to ask what was the driving force for the emergence of these secondary metabolites within plants during evolution? For many of these compounds and their respective pathways, the divergence of secondary metabolism was driven by the competitive advantage for those plants to avoid predation. Because animals were a conspicuous source of predation of plants, much of the secondary metabolism of plants evolved explicitly by Darwinian selective pressure to avoid being eaten by animals. Thus, quite the opposite of providing compounds to improve animal health, plant secondary metabolism evolved to produce compounds that were explicitly toxic to animals. Examples of the success of this evolutionary pressure abound, from soybean trypsin inhibitors to alkaloids.[12,13] Thus, although the plant kingdom and the rapidly arriving plant genomes are interesting targets for the development of knowledge of toxicity and anti-nutritive components, it is difficult to defend plants and plant metabolites *per se* as targets for healthful food structures.

To understand how to design food structures that optimize nutrient delivery, it is necessary to examine a food system that ideally was under Darwinian selective pressure during evolution to be explicitly nourishing in all its connotations. Fortunately, there is such a model, with remarkable complexity and genetic diversity – mammalian milk.

1.5 Milk as a Model of Food Structure and Nutrition

Milk is the only biomaterial that has evolved for the purpose of nourishing growing mammals. Survival of mammalian offspring has exerted a strong selective pressure on the biochemical evolution of the lactation process. Just as for evolution of any biological process, the strong survive at the expense of the weak, which leads to the appearance of new traits that promote health, strength, and, ultimately, survival. The same is true of milk. The role of milk was to produce the molecules that would ensure the survival of the mammalian offspring. The various processes of lactation have been described: the immature gland, the developing gland,[14] colostrum formation,[15] secretory activation (lactogenesis),[16–18] and involution and senescence.[19] The overall process of lactation requires extensive physiological, structural, and metabolic remodelling of the mammary tissue to enable it to acquire milk-forming capabilities.

This evolutionary pressure led to the elaboration of a whole food that contains proteins, peptides, complex lipids, and oligosaccharides in higher order structures, and all coming together as a complex, multicomponent – yet highly organized – food. In simple terms, milk is an obligate liquid. The basic mammary tissue constraints and the early evolutionary direction led to a liquid emulsion that had to stay in the liquid form to exit the ductal tissue and flow to the infant. Table 1 shows that the variation in milk composition is significant across mammals.[20] The composition of all of the macronutrients (protein, fat, and carbohydrate) vary significantly, with the extremes of protein being from ~1 to ~11 g per 100 g of fresh milk.

As milk has been studied more intensively, it has become evident that it is more than a simple repository of essential nutrients in a protein/fat/lactose 'broth'. Milk contains many compounds that exhibit properties associated with biological functions beyond simple provision of essential building blocks. Milk compounds and their configurations act as growth factors, toxin-binding factors, antimicrobial peptides, prebiotics, and immune regulatory factors within the mammalian intestine.[21] Gradually, science has found that these macromolecules deliver biological advantages to the intestine and throughout

Table 1 *Protein, fat, and carbohydrate composition of milk from different mammalian species (per 100 g fresh milk) (data taken from Ref. 20)*

Species	*Protein (g)*	*Fat (g)*	*Carbohydrate (g)*
Human	1.1	4.2	7.0
Monkey (rhesus)	1.6	4.0	7.0
Donkey	1.9	0.6	6.1
Goat	2.9	3.8	4.7
Cow	3.2	3.7	4.6
Elephant	4.0	5.0	5.3
Water buffalo	4.1	9.0	4.8
Mouse	9.0	13.1	3.0
Seal	10.2	49.4	0.1
Whale	10.9	42.3	1.3

the body, ultimately contributing to the survival of neonatal mammals.[22] It should be emphasized that research on these compounds and their functions is proving to be more difficult than traditional nutritional investigations on essential nutrients. Because these compounds and their functions are not essential, they have discernible value only to infants under certain circumstances. Hence, their functions, actions, and overall benefits have proven exceedingly difficult to recognize, and much less to study, and it is generally agreed that only a very small subset of the total biological value of milk's components is known.[23] Nonetheless, in study after study, the identification of component after component is revealing the evolution of milk as a highly functional food with properties that may find multiple applications to the structure manipulation of other foods. The evolution of the mammary gland was under constant Darwinian selection for the successful survival of offspring.[24] Milk is indeed a genomic model for the multidimensional aspects of nourishment.[25]

The evolutionary origins of milk proteins and mammary regulation define the key functions of milk and the mammary gland. The emergence during evolution of the mammary gland likely involved adaptive recruitment of existing precursor genes through alteration of regulatory sequences to allow expression in primitive mammary glands, and duplication and mutation of structural sequences to acquire new functions from pre-existing primitive proteins. Evidence is consistent with early precursors to lactation being derived from an ancestral apocrine-like gland that was associated with hair follicles that led to secretions designed to nourish and protect the soft, rubbery shells of egg-laying monotrenes.[26] The earliest mammary function after provision of nutrition was possibly the passing of protective advantages onto offspring *via* immunoglobulins, and thus aiding selection for survival. This would have paved the way for the elaboration of myriad protective functions that are only now beginning to be appreciated.

The functions of milk generally can be considered supportive of both mammalian mothers and infants through several mechanisms. Milk provides nourishment to infant offspring; disease defence for the infant; disease defence for the mother; regulation or stimulation of infant development, growth, or function; regulation or stimulation of maternal mammary tissue development, growth, or function; inoculation, colonization, nourishment, regulation, and elimination of infant microflora; and inoculation, colonization, nourishment, regulation, and elimination of maternal mammary microflora.

Nourishing the mammalian neonate is the most obvious role of milk, and the success of mammals attests to the value of milk as an initial food source for the young of these species. The demands on milk as a sole source of nutrition are remarkable. All of the essential macronutrients – water, vitamins, minerals, amino acids, and fatty acids – plus the basic structural and energetic intermediates needed to sustain life, must be delivered to the neonate in a highly absorbable form that is appropriate to the species and the stage of development – all at minimal energy cost to the mother. Lactation research has illuminated many of the biological processes needed to mobilize the essential biomolecules from maternal stores and to convert them into dispersed, transportable, and bioavailable structures in milk.

Milk also provides myriad benefits to the growth, development, and health-supporting processes of infant and mother beyond those of the essential nutrients. The nonessential components of milk as well as those of essential nutrients are not understood, but research is now beginning to focus on their roles in the well-being of neonates.[23] The research strategies needed to discover these properties are different from those used to discover the properties and roles of essential nutrients. The latter can be studied with relative ease because their elimination from the diet of animals leads to overt signs of deficiency in each individual. Nonessential nutrients and their functions, however, are only valuable within a particular context, and thus investigations of benefits of nonessential nutrients must first recognize the context in which they are valuable. This has become the great challenge for discovery of nutritional value of milk's nonessential components: when and why are they beneficial? Anything that is added to milk – literally anything – costs the mammalian mother; so, in a highly competitive environment, if it does not profit the infant, it would put the mother at selective disadvantage. Hence, it can be assumed that there was a selective advantage to the incorporation of the components in milk, and it is an exciting pursuit of modern nutrition to discover the biological value of each.

1.6 Bioactive Molecules in Milk

Milk is an excellent source of nutrients: high-quality protein, water-soluble and fat-soluble vitamins, calcium, phosphorus, magnesium, *etc*. But it is more than this. It is also a source of proteins with biological activities that have been demonstrated *in vitro*, in animal models, and in infant and adult humans. The physiological activities provided by milk proteins in the gastrointestinal tract include enhancement of nutrient absorption, enzyme activity, inhibition of enzymes, growth stimulation, modulation of the immune system, and defence against pathogens.[23,27–31]

Milk provides a myriad of defensive strategies for the intestine of the infant against exogenous pathogens, including immunological factors (antibodies, cells, cytokines), proteins (lactoferrin, enzymes, *e.g.*, lysozyme), oligosaccharides, and glycoproteins, gut microflora (prebiotics), and nutrients to optimize the infant's immune system, as reviewed in the recent literature.[32–35] Lactoferrin, lysozyme, and haptocorrin (a vitamin B_{12}-binding protein in human milk) have been proposed[36] to influence the growth of bacteria and elimination of particular pathogens. Although just beginning as a discrete field of nutrition, many of the intact milk proteins contain peptide sequences that appear to be expressly liberated by the proteases of intestinal digestion.[37]

With these multiple confirmations of milk's discrete biological functions beyond delivering simple calories, essential nutrients, and building blocks, milk is unquestionably a knowledge resource for nutrition. Millennia of Darwinian selective pressure have been guiding its evolution in many ways. Therefore, it is reasonable to interrogate the basic structures of milk for lessons on how to design molecular food structures for optimal nutrition.

1.6.1 Milk and Glucose Bioavailability

The rate of delivery of glucose has been under considerable scrutiny for several years because of the implications for adverse health of rapidly absorbed glucose from foods of high glycemic index.[8] It is thus potentially instructive to examine how glucose is, in effect, delivered in milk.

The vast majority of glucose is present in milk not as glucose, but as the disaccharide lactose. This is formed from glucose and galactose as a final step in the assembly of milk in the lactating epithelial cell. Lactose is a disaccharide that is strikingly non-digestible by humans. Only a single enzyme – lactase – has emerged through mammalian evolution to digest lactose, and this enzyme exhibits an equally remarkable regulation. This enzyme is produced by mammalian infants during the suckling period, and then, in virtually all mammals, this activity is down-regulated on weaning. Thus, intriguingly, mammalian mothers are unable to digest the lactose that they produce. Although various functions have been suggested for lactose's unique structure, there is one indisputable consequence of this structure to digestion. By delivering glucose in the form of lactose, mammalian evolution has placed the delivery of glucose exclusively under control of the infant and its lactase activity. Glucose will be digested and absorbed only as rapidly as the activity of its endogenous intestinal lactase enzyme allows. So, through the evolution of lactation, glucose is delivered as lactose, and this lactose invariably causes slow delivery of glucose.

1.6.2 Milk and Protein Bioavailability

The rate of delivery of protein has not been as well studied as that of other macronutrients, although recent research[38,39] has begun to examine variations in proteins as delivery agents for amino acids. Casein is the most abundant single protein source in most mammalian milks, and it is the protein component that is uniquely associated with milk.[29] Thus, it is interesting to examine casein structure for its nutritional value in terms of structure, digestion, and rate of absorption.

Proteins in general are digested by proteases as a consequence of their structure. In fact, all levels of protein structure – primary, secondary, tertiary, and quarternary – are known to affect proteolysis. The greater the degree of native structure, the less digestible is the protein. In general, denaturation of a protein increases its digestion by proteases. Thus, if evolutionary pressure were to be actively providing a selective advantage to highly digestible proteins, then the less the structure, the more digestible a given protein would be expected to be. Consistent with this interpretation, casein is perhaps the least structured protein known.[40] There is remarkably less secondary structure within any of the casein subunits. Thus, from this criterion of structure, casein would appear to be unusually susceptible to rapid hydrolysis by intestinal proteases. *In vitro* studies of protein digestibility have confirmed[41] that caseins are highly susceptible to proteolysis. This would logically lead to rapid digestion and absorption of the amino acids of casein proteins. Nonetheless, the casein proteins evolved with a quite remarkably distinct additional property. Assembled as multi-subunit complexes termed casein micelles, the caseins are actually large protein aggregates that, while soluble, are dispersible only in water, thanks to an exterior of predominantly hydrophilic κ-casein subunits. When the casein micelle encounters the mammalian infant stomach, one of the most ingenious events in nutrition occurs – the enzyme chymosin, expressed in the stomach of the infant, and with an acidic activity range, hydrolyses a single peptide bond on κ-casein. This reaction splits off the hydrophilic peptide of κ-casein (glycomacropeptide), which contains the surface-stabilizing element of the entire casein micelle. As a result, the balance of casein proteins within the stomach rapidly aggregates into a large, insoluble curd. This association process has the net effect of slowing the release, digestion, and absorption of casein's amino acids. Thus, mammalian casein has, in fact, a unique structure and structuring process that, at least in part, *slows* the delivery of milk protein.

1.6.3 Milk and Lipid Bioavailability

The digestion and absorption of lipids has been well studied from a wide variety of sources, including milk. There is a considerable challenge to the process considering the inherent insolubility of most lipids; thus, the conspicuous success of fat digestion by animals has been studied extensively. Although normally quite successful, several genetic and physiological defects in the intestine can lead to failures in fat absorption, termed steatorrhea. The difficulties that are presented by absorbing fat are the likely reason that fat is the most common form of intestinal malabsorption. Invariably, this clinical condition is highly deleterious, because of both the failure to absorb essential fatty acids and fat-soluble vitamins, and the loss of the substantial caloric density of dietary lipids. Therefore, there is considerable medical importance to ensuring that fat is in a highly absorbable form in milk.

Given the basic requirement to produce a fat globule for export into milk, there has existed in place, within the ancestors of mammals, some genetic motifs that were ostensibly 'available' to evolution of a fat-globule delivery system. The synthesis of lipoproteins was a well-established biological process in early animal evolution, with highly effective transport of intact fat globules being critical to the physiology of reptiles, amphibia, and fish.[42–44] These phospholipid-bound and apoprotein-targeted lipoproteins deliver triglycerides from the liver through the blood to the surface of various peripheral tissues in these organisms, and lipoprotein lipase activity on the endothelial surfaces is capable of very rapidly transferring the lipid contents to the targeted tissues.[45] Therefore, producing lipoproteins as fat globules in milk was an available alternative.

This is not, however, the structure of milk fat globules. Milk fat globules are simple, lipoprotein-like particles, as they are produced in the epithelial cell; but they do not acquire an apoprotein on their surface; and further, on exiting from the cell, each globule is enrobed with an intact coating of plasma membrane bilayer.[46] It is still perplexing to scientists as to why precisely this unusual course to milk fat structure evolved, but one thing has been determined. The hydrolysis rate of the milk fat globule is dramatically slowed by the presence of this additional plasma membrane bilayer.[47]

1.7 Food Structure and Nutrition – The Future

As a speciality within food science, the structure–function analysis of genetically defined biopolymers and their complexes has enormous potential in the coming decades. Previously, each field within the life sciences made progress within the narrow constraints of its particular discipline. Whereas there was sharing of the final outcomes (*i.e.*, confirmed or refuted hypotheses), the detailed information that was responsible ultimately for building the knowledge that they generated was only usable within each field. This perspective is now changing dramatically. Many fields of scientific inquiry are beginning to make progress in areas that produce information that, in its breadth, can be leveraged for the structure–function analysis of food materials. Given these technological innovations, an overview of what goals may be achievable is presented in Table 2.

To date, the most notable progress in structure–function analysis has been made with proteins. In the 1970s, the Brookhaven National Laboratory established the Protein Data Bank (PDB) as a repository for three-dimensional structural data of biological macromolecules.[48] A key aspect of this endeavour

Table 2 *From food structure to nutrition function: a vision for future decades*

Goal	*Key requirements*	*Fields to follow*
Establish function of known structure set	1. Standardization (structure format, experimental conditions, measurable end points) 2. Database development (repository)	Biochemistry, pharmacology
Establish function of synthetic structure libraries	1. Combinatorial synthesis of structures 2. Development of assays amenable to high-throughput screening	Chemical genomics
Establish individual response to structure	1. High-throughput screening for relevant polymorphisms 2. Optimization of food structure for specific profiles	Pharmacogenomics

was the use of a standard format, the PDB format, to represent structural data derived from X-ray diffraction and NMR studies. As of 13 June 2006, there were 37,136 protein and nucleic acid structures in the PDB database of the Research Collaboratory for Structural Bioinformatics (RCSB). Some more recently established databases, such as the Structure Function Linkage Database (SFLD), are integrating structural data with functional information.[49] The information in this database can be used for rule-based prediction of functional capabilities of new structures with unknown functions so long as the new structure is a member of a protein 'superfamily' in the database. The goal of food scientists must increasingly be to extend such annotations to include the structures and functions of proteins in food, and the diverse consequences of such structures when consumed for the relationship between diet and health.

While a database like the SFLD has had to be painstakingly assembled from the primary literature, the assembly of a food materials database could be accelerated if food scientists were to standardize experimental conditions and measurable end points at the outset. The integrity of inter-experimental analysis would also be improved. To some scientists, the need for a database may not seem immediately obvious. After all, new knowledge on the effect of a particular lipid structure on the glycemic index of a food bolus, for example, would be interesting in itself. But in the modern age of informatics, the data can be recycled from past experiments to generate and/or test hypotheses that could not have been conceived at the time of data collection. Furthermore, there remains the tantalizing proposal that the analysis of well-characterized known structures might help to predict the actions of unknown/unsynthesized structures.

Because it is unlikely that the predictive power of a few known structures will be sufficient to estimate the action of the infinite number of possible structures, food scientists may benefit from advances in chemical genomics. The objective of chemical genomics is to find those small molecules that interact with the genome. These molecules can then be used therapeutically as drugs or scientifically in experiments to better understand specific biological pathways.[50] The relevance to the science of food structure is that technologies for the combinatorial organic synthesis of small molecules may provide insight into methods for the combinatorial synthesis of food structures. Also, the application of creative labelling techniques, such as molecular tags,[51,52] could prove to be as useful in refining food biopolymer structures as they have proven to be for their biological counterparts.

To establish the functions of food structures in a fast and efficient manner, food scientists need to develop assembly systems and assays that are amenable to 'high-throughput' screening. At the cellular level, automated techniques have been developed for everything from microarrays to cell imaging. At the level of the organism, the means to measure metabolites in a high-throughput manner is already available.[53] Concentrations of various metabolites and fluxes between different body pools can be measured simultaneously. Elucidating the effect of food structures on the metabolome should lead to food products that have an influence on chronic diseases, and thus have a widespread impact on human health.

Finally, as the understanding of food structure–function relations in humans is improved, it is quite likely that responses to some food materials will be individual in character, *i.e.*, depending on a person's genotype. The emerging field of pharmacogenomics is likely to be the technology leader in this area. The goal of pharmacogenomics is to enable doctors to prescribe drugs on the basis of a person's genetic profile. To transfer this idea to food science, human genetic polymorphisms will need to be screened on a high-throughput basis to determine which of these may have an effect on a person's response to food materials. Then, ideally, food structures can be optimized for particular genetic profiles or for targeted nutritional goals.

1.8 Conclusions

The role of food structure in the nutritional value of diets is becoming recognized as being much more important than previously assumed. In fact, the examination of epidemiological associations between food structure and certain chronic and degenerative processes, from diabetes to macular degeneration, implicates the rate of nutrient delivery to be as important to health as the diet's overall macronutrient composition (protein, fat, and carbohydrate). Such provocative epidemiological results have prompted a re-examination of milk by asking the question: "how has the Darwinian selective pressure during evolution influenced the structure and delivery of milk components for infants?" Each component of milk – glucose, protein, and fat – although ultimately digestible and absorbable by the infant, is structured in such a way as to prolong its absorption rather than to accelerate it. These interrogations of milk are suggestive that the role of food structure should be an important part of all future diet and health research. Such a mandate would require that structural food chemists assemble the tools of food structure manipulation and examination expressly for use in nutrition-oriented studies. In essence, the fields of food structure, food chemistry, and nutrition must be reunited to consolidate the scientific depth and public health relevance of each.

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