Perspective: Reductionist Nutrition Research Has Meaning Only within the Framework of Holistic and Ethical Thinking

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ABSTRACT

Today, it seems that nutrition is in a state of great confusion, especially for the general public. For decades, some nutrients (e.g., cholesterol, saturated fats, sugars, gluten, salt) and food groups (e.g., dairy, cereals, meats) have been regularly denigrated. In this position paper, we hypothesize that such a state of confusion is mainly the result of the reductionist paradigm applied to nutrition research for more than a century, and by being pushed to its extreme, this perspective has led to accusations about some nutrients and foods. However, the real issue is about foods taken as a whole and therefore about their degree of processing, which affects both the food matrix and composition. Indeed, we eat whole foods, not nutrients. Therefore, the objectives of this article are to emphasize the need for more holistic approaches in nutrition to preserve our health, animal welfare, and planet. We propose to first redefine the food health potential on a holistic basis and then to show that reductionism and holism are interconnected approaches that should coexist. Then, we try to explain how extreme reductionism has been disconnected from reality and ethical considerations and has ultimately led to environmental degradation and loss of biodiversity, notably through very specific crops, and to an increased prevalence of chronic diseases. Furthermore, to address the confusion of the general public and to simplify nutritional messages, we propose 3 holistic golden rules based on scientific evidence to protect human health, animal welfare, and the environment (climate and biodiversity). Finally, we try to show how these 3 rules can be easily applied worldwide while respecting the environment, cultural traditions, and heritage.

Keywords: nutrition research, holism, reductionism, ultra-processed foods, chronic diseases, sustainability, biodiversity

Introduction

We eat foods, not nutrients. However, nutrients are regularly recommended to sell foods or are incorporated into national guidelines. “Eat less fat, salt, and sweets” is a well-known recommendation. In advertising, it is often the case to read: “rich in fiber, antioxidants, vitamins, minerals,” “low fat,” “reduced salt,” etc. On packaging labels, the only scientific information is that of nutrient composition, expressed by servings or on a 100-g basis. Nutrients and calories seem interchangeable from one food to another. This approach is called nutritionism or nutritional reductionism (1).

Gyorgy Scrinis (1) is probably the first to have clearly described and thoroughly analyzed the reductionist thinking in the nutritional sciences. Overall, he divided nutrition science into 3 eras since the beginning of research in nutrition, in ~1850: 1) the era of “Quantifying Nutritionism” (1850–1960s), controlled by research scientists who discovered and quantified nutrients, and human nutritional needs, notably leading to the prevention of nutritional deficiencies; 2) the era of “Good-and-Bad Nutritionism” (1960s–1990s), controlled by governmental bodies to prevent chronic diseases, with good and bad nutrients to be limited or encouraged, but negative messages dominated; and 3) the era of “Functional Nutritionism” (1990s until today), controlled by the agro-food industry with more positive messages for body health and a focus on functional nutrients.

However, despite the vast knowledge in nutrition science, the prevalence of chronic disease continues to dramatically increase worldwide, with the WHO predicting that type 2 diabetes will be the seventh cause of death worldwide by 2030 (2). Did we fail somewhere or do we truly lack more knowledge? In addition, the general public is in a state of great confusion about nutrition recommendations or guidelines. We first accused fat (notably cholesterol and SFAs) as a cause of cardiovascular diseases; then, sugars were thought to increase the prevalence of obesity and type 2 diabetes; then, salt was linked to hypertension; and today, some reject gluten, cereals, dairy, etc., advocating
a return to the Paleolithic diet (3, 4). At the same time, new scientific studies have rehabilitated cholesterol (5), saturated fats (6–8), butter (9), and eggs (10). Who is right? Who is wrong? Vegans, vegetarians, flexitarians, or omnivores? Everybody? Are there intangible truths in human nutrition science?

The hypothesis we would like to defend in this position paper is that such confusion is the result of the reductionist paradigm pushed to its extreme, and that has led to accusing some nutrients, whereas the real issue is about foods taken as a whole and therefore about their degree of processing that affects both the food matrix and composition. The objectives are to emphasize the need for more holistic approaches in nutrition to preserve our health, animal welfare, and our planet. We propose to show, first, that reductionism and holism are interconnected approaches that should coexist. Then, we will try to explain how reductionism has led to environmental degradation and an increased prevalence of chronic diseases; and we will propose 3 holistic golden rules based on scientific evidence to protect health, animals, and the environment. Finally, we try to show how these rules can be easily applied worldwide while respecting the environment, cultural tradition, and heritage.

**Holism and Reductionism: Two Sides of the Same Coin**

**What is food health potential?**

We are used to defining food health potential on the basis of the mere nutrient composition of the food. By looking at food-composition databases, such as those of the USDA (11) or the French Agency for Food, Environmental, and Occupational Health and Safety (12), or by looking at food packages or food indexes, it is apparent that they are only based on a few nutrients to limit or encourage [e.g., the British Food Standards Agency Nutrient Profiling System (13) or the Nutrient-Rich Food index (14)]. In nutrient databases, the list of main nutrients is generally as follows: water, calories, protein, lipids, carbohydrates, sugars, fiber, sugars, and sometimes vitamin and mineral composition. We also mention the recent Phenol-Explorer database, which is the first comprehensive database on polyphenol content in foods (15). In these lists or databases there is no information about food matrix characteristics that greatly affect nutrient bioavailability, digestion kinetics, and glycemic, satiety, antioxidant, or alkalinizing potentials. However, 2 foods with same composition but with different matrices may have a different health potential (16), especially concerning the satiety effect and nutrient bioavailability.

For example, according to particle size, such as whole compared with ground, almonds release their lipid fraction differently with respect to the kinetics of hydrolysis and the amount of lipid reaching the colon (17, 18). In this case, the initial composition is exactly the same. Concerning bread, it has been shown that the higher the crumb density, the lower the glycemic index and the higher the satiety potential: again, the composition is approximately the same; only the crumb density varies (19). In another study, boiled whole carrots lead to a greater feeling of satiety than reconstituted carrots from isolated nutrients (but without fiber) (20). Another example involves pasta: at an identical composition but with a different form or thickness, the glycemic response differs, with macaroni having a greater glycemic index than spaghetti (21), and thick linguine having a greater glycemic index than thin linguine (22). Again, the composition does not change. Concerning fruit, a whole apple was shown to provide a significantly lower insulminemic response and greater feeling of satiety than apple purée made of the same apple. In addition, apple purée was shown to provide a significantly lower insulminemic response and a greater feeling of satiety than apple juice made of the same apple (23). In this study, the main factor of variation is the unstructuration of the apple matrix. Finally, concerning dairy products, different gels (acidification compared with renneting) of identical initial composition lead to different protein bioavailability and metabolization and different kinetics of satiety and appetite hormone secretion (24).

The food matrix effect is therefore of prime importance in defining food health potential because it plays a role not only on feelings of satiety (25) and nutrient bioavailability (26, 27) but also on the degree of chewing (25) and particle size after chewing (28), hormonal secretions (24), transit time (notably gastric-emptying kinetics) (29), or the amount of fiber-type compounds entering the human colon with important metabolic effects via microbiota transformation in SCFAs (30) or via antioxidant release (31), among other effects.

These results clearly show that food health potential must be redefined using a new paradigm including both “matrix” and “composition” effects or, expressed differently, the “holistic” and “reductionist” parts of food (Figure 1). The holistic fraction of food is its matrix, resulting from the specific interconnectedness of the various nutrients, which is specific for each food comprising a diet. This fraction controls the delivery and ultimately the bioavailability of various nutrients within the human organism. This fraction may be qualified or characterized by both quantitative and qualitative aspects, such as color, density, hardness, or size. When the matrix is fractionated, we can have access to the nutrient composition and quantify it: this is what we call the reductionist and quantitative fraction of food health potential. On the basis of the scientific literature, we propose that the matrix effect takes precedence to define health potential, then nutrient composition follows because we first eat food matrices not nutrients (33). In addition, nutrients are included in the matrix, not the contrary. Consequently, in the following sections, we try to show that reductionist studies have meaning only within the framework of holistic thinking, and we think this applies to foods.

The consequences of redefining food health potential on the basis of both “matrix” and “composition” effects are fundamental: the first is that calories and nutrients...
are absolutely not interchangeable from one food to another. It is not the same for health endpoints to consume 500 kcal of “empty” calories from ultraprocessed foods as it is to consume 500 kcal of minimally processed whole foods. In addition, it is not the same to consume industrial fructose from high-fructose corn syrup as to consume natural fructose from whole fruit and honey that also supply fiber, minerals, vitamins, antioxidants, a feeling of satiety, etc. The real issue is not in the nutrient in itself but in its matrix environment, which, in turn, is greatly influenced by processing.

This leads to the concept of the holistic view of food health potential. Foods, when based on scientific results, should be viewed as a whole, not as a collection of parts (i.e., isolated nutrients), and whole foods have different health properties than do fractionated-recombined foods, even those of similar composition. Therefore, nutrients act differently within the human organism when included in natural matrices than when added in artificial matrices from ultraprocessed recombined foods. Indeed, when present in natural whole foods, polyphenols, minerals, oligo-elements, vitamins, and other phytonutrients act in synergy, with the synergy being generally lost when these nutrients are extracted from their initial matrix and incorporated into artificial matrices (34, 35). This is particularly true for antioxidants that are efficient within the human organism in synergy but not in isolation.

There are also technological consequences. On the basis of this new definition or paradigm of the food health potential, technologists or food scientists will likely be more respectful of the food matrix as a whole and search for less drastic processes, such as minimal processing, to preserve the positive health effect of the whole food matrix. Until today, the focus has been mainly on the impact of processing on the nutrient composition of foods, not so much on the matrix. However, if processing may decrease (e.g., mechanical and thermal treatments) or increase (e.g., fermentative treatments) some nutrient content, it may also affect the food matrix (e.g., un structuration through fractionation/refining or cooking). However, the equation is very complex to study because a food may be the result of several technological treatments, each one having different effects on each of the nutrients contained in the foods. This double complexity renders the study of the impact of processing on food health potential difficult. For example, yogurt results first from milk homogenization and sterilization and then from fermentation; thus, although thermal treatment decreases vitamin B content, fermentation may increase the folic acid content.

Reductionism compared with holism: an indispensable marriage

Reductionism and holism are both indispensable because they both proceed from reality but according to different “entrance doors” or points of view (Figure 2A). Expressed differently, both approaches are not mutually exclusive: this is an indispensable marriage. However, today, we tend to make 2 errors in nutrition research, as follows:

1) One goes from reductionism to holism as shown by the reduction in food health potential to 1 or 2 nutrients: for example, citrus and ascorbic acid, meat and protein (which suggests that vegetables do not contain proteins), whole-grain cereals and fiber, dairy and calcium (which suggests that other foods do not contain calcium), etc. Actually, all whole foods are a complex set of hundreds of nutrients.

With identical composition in nutrients and calories, two foods with different physical structures will not have the same health potential

1 calorie food A ≠ 1 calorie food B

Consuming 500 kcal from minimally-processed foods does not have the same effect on health as 500 kcal from ultraprocessed food

FIGURE 1 The 2 components of the food health potential. Reproduced from reference 32 with permission from Academic Press.
2) One places too much emphasis on reductionism, which tends to be dogmatic and turns back on itself, disconnected from holistic thinking, ethical considerations, and real life (Figure 2B). We can thus lead reductionist nutrition studies but having lost the initial purpose (e.g., providing scientific data and unraveling truths serving society, humans, and the environment); not to the benefit of innovation considered as a dogmatic truth. Food and nutrition innovations are not value-creating in themselves: they become value-creating only if they register in a virtuous holistic circle to the benefit of humans and the environment (Figure 3). Campbell and Jacobson (36) have well described and analyzed this point in American nutrition research: reductionism used partial scientific truths obtained from reductionist experimental design(s) to make as much money as possible. Reductionist science, used for innovation and immediate benefit, always promises the general public rapid and magic solutions in the short term, whereas holistic scientific evidence takes time to be discovered and is not aimed at profitability; it is based on global and realistic scientific results for the benefit of humans in a holistic virtuous circle (Figure 3).

Therefore, we propose that a change should be made in the following way: first, think holistically; then, lead reductionist studies only if they nurture the holistic issue in a virtuous way.
to the benefit of humans, society, and the environment as a whole.

Some examples where reductionism was erroneously privileged over holism

In the history of nutrition research, there are several examples where reductionism was privileged over holism, leading to partial scientific results exploited by the private agro-food industry but with no substantial benefit to society. The first example is the protective nature of whole grain–based products (37, 38). Scientists have studied cereals’ health potential in a reductionist way by progressively dividing it into its isolated compounds and trying to explain its health potential through only a few bioactive compounds. First, there was the “fiber hypothesis”; then, the role of resistant starch, slow carbohydrates, minerals, vitamins, polyphenols, and antioxidants were isolated; today, choline and betaine are distinguished (38). However, this is the whole-grain cereal matrix, and the synergy between bioactive compounds which is protective, not only as one or a few compounds (e.g., whole-grain cereals contain >30 different antioxidant compounds, >10 lipotrophic compounds (39), and hypocholesterolemic, ant carcinogenic compounds, etc. (37, 38)). The best way to analyze the potential health protective nature of whole-grain cereals should be first to study how whole grains are protective in a complex diet, including both the matrix, synergy, degree of processing, and compositional effects, and then, if truly necessary, to lead more reductionist research to better understand the role of specific compounds, such as fiber or others on different metabolic pathways but within the framework of holistic thinking and issues (37).

Dividing whole-grain cereals into several bioactive compounds has led to marketing reconstituted whole-grain products, such as whole-grain soft bread or whole-grain breakfast cereals for children, which remain ultraprocessed foods without the same health effect as minimally processed and not unstructured whole-grain foods.

Another relevant example, described by Gyorgy Scrinis in “Nutritionism” (1), is the “low-fat campaign” launched in the United States in the 1960s (40). Confronted with an increase in cardiovascular disease prevalence, the US government asked scientists to find the cause of this. An American scientist thought fat was the cause, whereas a British scientist thought it was sugar. The battle lasted several years until the “fat hypothesis” won. After this, the government asked the agro-food industry to market low-fat foods and they launched the famous “low-fat campaign.” Unfortunately, it was after this campaign that obesity prevalence exploded in the United States because fat in foods had been replaced by other ingredients, notably by added simple sugars. This is typical of the reductionist approach, which searches for the cause of disease in one nutrient. The real issue was not fat or sugars but the vehicle of these nutrients—that is, increasingly ultraprocessed foods made of fractionated-recombined ingredients. The solution was holistic, not reductionist. With reductionism, we think about finding the right solution but we often worsen the situation. This is evident by considering how obesity and type 2 diabetes prevalence have increased worldwide despite the vast amount of reductionist knowledge we have accumulated during the past 7 decades after World War 2.

Unfortunately, most nutritional guidelines worldwide were reductionist. For example, in France, we have “Eat less sugar, salt, and fat” instead of “Eat less ultraprocessed foods,” which is a holistic recommendation. As previously discussed, we do not eat sugar, salt, or fat but more or less processed foods. More generally, in the near future, the real issue of national guidelines should be a holistic issue, highlighting diet sustainability—that is, recommendations that should protect human health, animal welfare, and the environment. Things are going to change, but we are still far from it.

Finally, it is relevant to emphasize that the “dietary pattern approach” that is used in epidemiologic studies since the beginning of this century is more holistic than the “nutrient or food approach” (that prevailed before the year 2000), linking the prevalence of chronic diseases with the consumption of a given nutrient or food such as SFAs, cholesterol, simple sugars, vitamins, and minerals. Indeed, the current view is an admission that the onset of a chronic disease is more in line with a lifestyle than with a single nutrient. However, this “single nutrient” approach was privileged for a long time in epidemiology, leading to ineffective national nutritional guidelines that are still used today. It is therefore not surprising that now nutritional dogmas about single nutrients or single foods (i.e., eggs, butter, cholesterol, SFAs, etc.) are challenged one after the other.

The importance of the reductionist view of foods

When included in holistic thinking, the reductionist view of food may then be very useful in research. For example, since the beginning of nutrition research in the mid-19th century (~1850) the discovery of main nutrients, especially vitamins, has clearly allowed the prevention of deficiencies, saved millions of lives, and unraveled nutritional needs for each macro- and micronutrient. It is also necessary to understand how nutrients act in the human organism and what are
their metabolic fates and actions in cells and on genes, on hormones, etc. This is indubitable, and a reductionist approach is necessary. Other benefits of reductionism have shown the importance of not exceeding some levels of omega-6 FAs, SFAs, added sugars, or free sugars in our diet.

**Reductionism and Food System Sustainability**

Now, we would like to move from a holistic vision of food health potential toward a holistic vision of diet sustainability because the concept of "sustainability" is closely linked to holism. In other words, "sustainability" in all its dimensions can be reached only if we move toward more holistic approaches of diets and food systems, including the holistic concepts of "synergy," "interdependence," "biodiversity," etc.

**The different dimensions of sustainability**

A sustainable food system should address several dimensions of sustainability (41): 1) sustainable health—that is, a long life but a healthy long life with an increase in the health life years (or years without disabilities), which is not the case (42); 2) sustainable socioeconomics, including the access of healthy and affordable foods for everyone regardless of socioeconomic status, including fair and equitable trade worldwide, which again is not the case; 3) animal welfare and diversity, including animal respect and not reducing animal species to only 2 or 3 genetic types for making profitable meat and milk production; 4) food safety, which has reached a very high level in Western countries; 5) environmental sustainability, including the issues of climatic change, pollution, and loss of biodiversity; and 6) cultural sustainability, which involves respecting traditional culinary heritages and cultures: thus, when standardized junk-food, ultraprocessed, and fast-foods are substituted for traditional dishes, culture and tradition sustainability is threatened to the point that fast-foods may become a new cultural standard, notably among the youngest. Clearly, sustainability is a holistic scientific issue. This means that a food should be not only good for human health but also, at the same time, good for animal welfare, traditions, the environment, etc.

**Reductionism, ultraprocessing, and chronic diseases**

Actually, the explosion of chronic disease prevalence worldwide—threatening the number of healthy life years—is the result of the reductionist approach (Figure 4). Reductionist thinking has led to fractionating natural foods offered by nature into isolated entities (i.e., industrial ingredients such as gluten, modified starches, glucose and fructose syrups, protein isolates, inverted sugars, fiber, minerals, vitamins, antioxidants, concentrates); the sum of isolated nutrients or ingredients is now largely more profitable than the original whole foods. In addition, often these ingredients are also processed (i.e., extracted, purified, and hydrolyzed). Then, ingredients together with industrial additives are recombined to provide ultraprocessed foods, nutritional supplements, functional foods, or nutraceuticals.

The term “ultraprocessed food” first appears in the scientific literature in 2009 (43). Brazilian epidemiologists define it as follows (44, 45):

> “These are industrial formulations typically with five or more and usually many ingredients. Such ingredients often include those also used in processed foods, such as sugar, oils, fats, salt, anti-oxidants, stabilizers, and preservatives. Ingredients only found in ultra-processed products include substances not commonly used in culinary preparations, and additives whose purpose is to imitate sensory qualities of unprocessed or minimally processed foods or of culinary preparations of these foods, or to disguise undesirable sensory qualities of the final product. Natural foods are a small proportion of or are even absent from ultra-processed products. Substances only found in ultra-processed products include some directly extracted from foods, such as casein, lactose, whey, and gluten, and some derived from further processing of food constituents, such as hydrogenated or inter-esterified oils, hydrolyzed proteins, soy protein isolate, maltodextrin, invert sugar and high fructose corn syrup. Classes of additive only found in ultra-processed products include dyes and other colors, color stabilizers, flavors, flavor enhancers, non-sugar sweeteners, and processing aids such as carbonating, firming, bulking and anti-bulking, de-foaming, anti-caking and glazing agents, emulsifiers, sequestrants and humectants. Several industrial processes with no domestic equivalents are used in the manufacture of ultra-processed products, such as extrusion and moulding, and pre-processing for frying.”

Therefore, ultraprocessed foods result from reductionist nutrition or nutritionism as described by Scrinis (1). In other words, they are the fruits of reductionist thinking considering foods as only the sum of interchangeable nutrients and calories. For most of them, these products are “empty” calories with a high nutrient-to-limit index (>8 for many of them) (46) and a high number of ingredients (>4) (16), devoid of bioactive and protective fiber, micronutrients, and phytonutrients; and, as expected, they therefore have a poor nutritional density (16, 47, 48). In addition, they are also generally hyperglycemic and poorly satiating according to a transitive relation, as described in Figure 5 (16, 47, 49). Indeed, we statistically showed in 145 foods that the more the food is unstructured/processed, the higher the glycemic index, and the less its satiating capability (47, 49).
A high consumption of ultraprocessed foods has also been associated with increased body fat during childhood and adolescence (50) and increased risk of metabolic syndrome (51, 52), obesity (53), dyslipidemia (54), and hypertension (55), which may lead to more severe chronic diseases, such as cardiovascular diseases and some cancers (56).

**Food system sustainability and reductionism**

Therefore, it seems that there is a close link between reductionism, ultraprocessed foods, and chronic diseases (Figure 4). In addition, these foods are processed and recombined from industrial ingredients massively produced worldwide from monocultures and industrial farming via food splitting and threaten biodiversity (e.g., soybean, wheat, maize, milk, and eggs). Fractionating natural foods into numerous ingredients and then recombining them to produce standardized worldwide ultraprocessed foods indeed results in cheap products but is expensive for both our health and environment. Consequently, there is also a narrow link between reductionism, massive monocultures, loss of biodiversity, environmental threats, and ultraprocessed foods and chronic diseases. This equation, based on reductionism, should be strongly addressed. Furthermore, the industrial meat that can be found in ultraprocessed foods generally comes from intensive animal farming that is disrespectful of animal well-being. After all, we take the lives of animals to prolong ours; therefore, the least we can do is to respect them (i.e., their natural needs) until their slaughter. Our Western diet, high in animal and ultraprocessed calories, emanates from reductionist thinking and is therefore costly for both human health and the environment and even more costly when adding public health costs.

An important issue arises: Is there a unique cause to environmental degradation, intensive animal farming, and chronic diseases? We hypothesize that reductionism pushed to its extreme is this unique, at least the first, cause. Intensive conventional monocultures and animal farming for massive and cheap food ingredient production for ultraprocessed foods decrease both plant and animal biodiversity and produce high quantities of greenhouse gases. Concerning breeding, only a few species are selected for their ability to produce as much milk or meat as possible. For a century now, 75% of plant species have disappeared according to estimates by the UN FAO (57). The proof of this massive standardization of cultures is that today only 150 species of plants feed the planet, against the tens of thousands of plants cultivated since the birth of agriculture. Among the 150 species, only 12 plants and 5 animal species account for 75% of the world’s food. This standardization of agriculture weakens cultures and increases the problem of preserving biodiversity.

In contrast to monocultures, biodiversity involves holistic thinking, recognizing interdependence between all entities—humans, animals, and the environment—with each one sustaining the other: for example, within the plant kingdom, the association of cereal and pulse crops leads to less use of chemical fertilizers. Although reductionism fractionates a complex reality, holism is based on the links between entities. As a result, consuming less-processed foods (i.e., not fractionated-recombined and ultraprocessed foods) may stimulate biodiversity in our diet, in animal breeding, and in the environment. Today, we have developed, from farm to fork, reductionist and unsustainable agronomic value chains. Developing sustainable food systems likely involves returning to more holistic approaches, recognizing interconnect- edness between humans, animals, and the environment. One should not forget that, in the past, philosophy was strongly associated with science: for example, the reductionism of Descartes applied to science. Therefore, the same can be done with holism.

On the basis of holistic thinking, we now propose what we call “the 3 golden rules for healthy, ethical, and sustainable diets.” Indeed, these rules could not flow from reductionist thinking as is the case today (i.e., an approach based only on the composition or calorie contents of foods).

**A Proposed Holistic Solution: The 3 Golden Rules to Preserve Human Health, Animal Welfare, and the Environment (Biodiversity and Climate)**

The 3 golden rules encompass all former reductionist nutrition recommendations based on the nutrient approach only, but when applying them we also protect human health, animal welfare, biodiversity, and the environment (pollution, biodiversity, climate, etc.). In French, they are the 3 Vs for “Végétal, Vrai (aliment), Varié” or “Plant, Real (food), Varied.” In other words, they intend to include nutrition science, even nutrient composition, using holistic thinking and to naturally fulfill our nutritional needs without worrying about them. Another important point is that these 3 rules are all mutually inclusive and should be applied.
together, not only singly; the first rule without the 2 others is meaningless.

More generally, all nutritional sciences, whether in vitro or in vivo, both in animals and humans, converge toward a universal protective diet—that is, a diet rich in minimally processed and varied plant-based foods. In addition, it is relevant to observe that all complex protective diets are rich in minimally processed and diversified plant-based foods and basically fulfill the 3 golden rules. These are notably the Okinawan (58), prudent (59), vegetarian (60), and Mediterranean (61) diets.

**Rule 1: a minimum of 83% of calories from plant origin**

"Prefer plant products to animal products in a caloric ratio of ~83% to 17% (i.e., no more than 1 calorie out of 6 of animal origin."

Scientific evidence strongly suggests that we must reduce the consumption of animal calories, especially red meat, for protecting both health and the environment (56, 62–67). Many dietary patterns with less meat than in the classic Western omnivorous diet have been associated with lesser prevalence of chronic diseases and their risk factors, such as vegetarian (68), flexitarian (69), Mediterranean (70, 71), prudent (72), or Okinawan diets (58). Thus, a Dutch study has reported that a one-third substitution of meat (all meats combined) with other foods (vegetables, cereals, fish) significantly increased survival rates (6–19%) after 16 y in a cohort of 40,011 subjects, and reduced greenhouse gas emissions (4–11%) and land use (10–12%) (73). All the above-mentioned diets are characterized by less or no meat at all and overall fewer animal calories than the Western diet. For example, the vegetarian diet recommends 2–3 servings of dairy products or eggs/d; the flexitarian diet recommends 1–2 servings of fish and meat/wk; the Okinawan diet suggests 3–8 servings of animal products/wk, excluding meat; and the Mediterranean diet recommends 3.5 servings of animal products/d. In addition, epidemiologic studies show that adherence to a diet rich in minimally processed plant products is good for health and decreases the risk of metabolic dysregulation and the chronic diseases of industrialization (56, 74–77). As we suggested previously, the recommended daily percentage of animal calories should protect human health, animal welfare, and environmental biodiversity and climate. What could be this percentage worldwide for the future? On the basis of the above protective diets, it seems reasonable not to exceed 2–3 servings of animal products/d.

In 2009, the prospective French National Institute for Agricultural Research or Institut National de la Recherche Agronomique; Cirad is Centre de coopération internationale en recherche agronomique pour le développement (INRA-CIRAD) "Agrimonde" report (78) proposed a trend-breaking scenario (Agrimonde 1) to achieve worldwide sustainability of our food systems and properly feed the world population by 2050 (probably 9.1 billion human beings)—that is, our agricultural environment should provide ~2500 kcal · d⁻¹ · inhabitant⁻¹ from plants (83%) and ~500 kcal · d⁻¹ · inhabitant⁻¹ from animals (17%), including the calories that are lost between the purchase of products and their ingestion. The assumption of food availability retained for 2050 is therefore 3000 kcal · d⁻¹ · inhabitant⁻¹ in all regions of the world while maintaining certain regional specificities, perceptible in the decomposition of animal calories by source (monogastric, ruminants, and fish products). Currently, food availability varies between 4500 kcal · d⁻¹ · inhabitant⁻¹ for the United States and <2500 kcal · d⁻¹ · inhabitant⁻¹ for sub-Saharan Africa. In the United States and in all developed countries in general, on the basis of 4500 kcal · d⁻¹ · inhabitant⁻¹ provided by agriculture, 800 kcal are lost in the field (diseases, insects, storage, etc.), and 1500 kcal are dedicated to feeding animals, which only restores an average of 500 kcal on the plate. Then, 800 kcal are still lost in waste.

A percentage of 17% of animal calories/d is globally in agreement with the number of servings of daily animal-based foods encountered in the protective complex diets cited above (i.e., 2–3 servings/d). For example, the daily consumption of 1 serving of cooked egg, cooked fish/beefsteak, and yogurt amount to ~20% of calories from animals.

This implies, for countries that consume a high amount of animal calories—generally, >25% for many developed countries (79)—that they need to decrease by at least one-third their animal calorie consumption. This could be advantageously reached by replacing them with grain-, seed-, and nut-based foods, mainly whole-grain cereals/pseudocereals (rich in complex carbohydrates), legume seeds (rich in proteins), and nuts (rich in lipids), which are underconsumed in the major developed countries [the replacement by fruit and vegetables, if desirable for health, has been shown to be largely less sustainable, notably in terms of greenhouse gas emissions (80)]. For example, in France, their consumption is <14 (81), 8 (82), and 4 (82) g/d, respectively. In addition, these grains and seeds are sustainable, easy to store for a long time, and rich in low-glycemic and fiber, minerals, and vitamins, and the combination of cereals and legumes is well known to supply all essential amino acids, as in animal-based products. In addition, due to their solid matrix, they are generally considered as quite satiating (83–85). This way of eating is similar to the currently available flexitarian or semi-vegetarianism diets. The increasing number of the consumers of these new diets is an indicator that demand for healthier foods is increasing, and public policies may help by providing support to producers and retailers.

It seems that a ratio of 83 to 17 would also be in agreement with the calculated reduction in animal calories to reach substantial greenhouse gas reduction. Perignon et al. (86) wrote in a recent review about this issue: "Reductions in meat consumption and energy intake were identified as primary factors for reducing diet-related greenhouse gas emissions. The choice of foods to replace meat, however, was crucial, with some isocaloric substitutions possibly increasing total diet greenhouse gas emissions."
Green et al. (66) reported in 2015: “Our dietary optimizations show that emissions reductions can be achieved by reducing consumption of animal products, switching to meats and dairy products with lower associated emissions (e.g., pork, chicken, and milk), reducing consumption of savory snacks, switching to fruits and vegetables with lower emissions, and increasing consumption and cereals. The optimized diet stops short of suggesting that the universal adoption of vegetarianism or veganism is essential (which will not be currently acceptable to large sections of the population).” To reach a 60% reduction in greenhouse gas emissions, they calculated a drastic reduction in animal-based foods: 50% for red meat, 33% for white meat, and 50% for eggs and dairy products. In another study about the western Dutch diet, it was reported that a sustainable healthy consumption scenario would involve a reduction of ~65% for red meat, ~56% for fish, and ~22% for cheese consumption (63). In addition, greenhouse gas emissions from foods were shown to be inversely related to the healthfulness of the diet (87, 88). Furthermore, a recent systematic review reported that reductions in environmental footprints were generally proportional to the magnitude of animal-based food restriction (64).

A few words about animal welfare are also necessary: there is no need to show that by reducing our animal calories we will consequently relieve animal intensive breeding through restriction of demand. Although it can be accused of bias, because of its militant reputation, the CIWF (Compassion In World Farming) considers that ~2 animals out of 3 are bred in intensive conditions worldwide, and these conditions are often unrelated to animal welfare. The idea behind animal-based food reduction is that, for the same price, animal products of better quality and often derived from better breeding conditions, such as organic or extensive ones, can be consumed.

However, it seems that there are exceptions to this first golden rule: the diets of the Inuit and Masai are rich in animal calories. Although they have a lower life expectancy than Western populations, it is difficult to ascertain whether or not this lower life expectancy is linked to the nutrition transition—characterized by a decline in the consumption of nutrient-dense traditional foods originally gathered by Inuit from their local environment, concurrent with an increase in the consumption of non–nutrient-dense/energy-dense market foods (89–91)—or whether other factors linked to medical care overall are involved. They are, however, an exception, and they have adapted to their specific environment, which cannot be extrapolated to >9 billion people in 2050. In addition, the Inuit have a unique genetic mutation that acts on metabolism and provides for neutralizing the negative effects of a diet rich in marine mammal fats (i.e., fatty seafood), their main source of foods (92). Concerning the Maasaï’s traditional diet, it consists of blood, milk, animal fat, honey, and tree bark (93). They are only a few of those who are affected by chronic diseases, especially cardiovascular diseases (94). Then, once infant mortality has been overcome, their life expectancy is similar to that of those in developed countries. However, although being rich in animal calories, both the Maasai and Inuit diets are characterized by minimally processed foods.

**Rule 2: a maximum of 15% of calories from ultraprocessed foods**

“Within plant and animal products, emphasis should be given to unprocessed, minimally or (normally) processed foods (i.e., foods which are not a recombination of ingredients already isolated from complex natural foods by fractionation or cracking) in a ratio of 85% to 15%, meaning no more than 1 calorie out of 6 from ultraprocessed foods.”

Since the end of the World War 2, the entire world has been undergoing a great nutritional transition: the transition from normally to ultraprocessed products (95), which culminated in the 1980s (96). It is the first time in the history of mankind that we have subjected our bodies to such a large extent to artificial food matrices and to so many ingredients and additives of strictly industrial origin. When regularly consumed, ultraprocessed foods become deleterious to health, and even more so when they constitute the basis of our diet (44, 50–55). Therefore, it is logical to advise not to consume too much of these foods, whether they are derived from plant or animal origin. In addition, it has been recently shown that the increase in servings of ultraprocessed (termed “unhealthy” in the study) plant-based foods increases the risk of coronary heart diseases in the same way as the increase in animal-based foods (97). However, which ultraprocessed calorie percentage to follow as a daily limit is even more difficult to precisely specify. However, some studies led worldwide, notably with the international NOVA (“new” in Portuguese) food classification, may provide an approximate and first estimate of this percentage.

In the first cross-sectional study, the amount of ultraprocessed calories consumed was calculated in 30,243 individuals aged ≥10 y from the 2008–2009 in the Brazilian Dietary Survey (53). After multivariate adjustment for the risk of being obese, there was a significant increase of 29% beyond the 13% of calories from ultraprocessed foods (% of total energy), that of being overweight significantly increased by 17% beyond the 22% of calories from ultraprocessed foods (% of total energy), whereas BMI significantly increased by 0.33 beyond the 13% of calories. In the second cross-sectional study performed in 55,970 Brazilian households, the authors observed a significant and positive linear trend across quartiles of calories of ultraprocessed products (P < 0.001) for overweight, obesity, and mean BMI (z score) (i.e., from 220.0 to 564.3 kcal/d) (98). In the third cross-sectional study performed in 210 Brazilian adolescents, high consumption of ultraprocessed foods (>1245 g ultraprocessed foods/d) was significantly (P = 0.012) associated with the prevalence of metabolic syndrome (51). These results were confirmed in an indigenous Cree (Eeyouch) population in northern Quebec, in which only the dietary intake of ultraprocessed products was significantly associated with metabolic syndrome risk.
(52). Then, in a recent prospective study in 345 children of low socioeconomic status, the data suggest that early ultraprocessed product consumption (>33% total energy intake) played a role in altering lipoprotein profiles between 3–4 y (preschool) and 7–8 y (school age) (54). The percentage of daily energy provided by processed and ultraprocessed products was 42.6% ± 8.5% (mean ± SD) at preschol age and 49.2% ± 9.5% at school age, on average.

In the same way, a systematic review that included 26 studies concluded that most studies found positive associations between the consumption of ultraprocessed food and body fat during childhood and adolescence (50). Conversely, among 302 Lebanese adults, participants in the highest quartile of the “minimally processed/processed” (quantity not given) pattern had significantly lower odds for metabolic syndrome (OR: 0.18; 95% CI: 0.04, 0.77), hyperglycemia (OR: 0.25; 95% CI: 0.07, 0.98), and low HDL cholesterol (OR: 0.17; 95% CI: 0.05, 0.60) (99). Furthermore, the recent Nutrinet cohort study reported that “a 10% increase in the proportion of ultraprocessed foods in the diet was associated with a significant increase of greater than 10% in risks of overall and breast cancer” and conversely an increase of 10% minimally processed foods was associated with a reduced risk of 9% overall cancer (100). In another Spanish cohort [the Seguimiento Universidad de Navarra (SUN) project] who was free of hypertension at baseline, a significant increase of 21% in the incidence of hypertension risk was observed after 9.1 y in the tertile consuming 5.0 ± 1.7 servings of ultraprocessed foods/d as defined by NOVA (55), with a significant linear trend (P = 0.004) from 2.1 to 5.0 servings/d. Within the same SUN cohort, this research team also calculated that incident overweight and obesity significantly increased by 15% as soon as an average of 2.7 servings of ultraprocessed foods/d (P-trend = 0.001 for the quartiles) (101) was reached. Finally, Moreira et al. (102) recently calculated that cardiovascular disease mortality might be reduced by 29% via reducing the intake of saturated fat, trans fat, salt, and added sugar from ultraprocessed foods by 75%.

Although further studies are obviously needed, notably prospective cohort studies, it seems that as soon as the daily intake of 13% of calories from ultraprocessed foods is reached, the obesity risk may begin to significantly increase (53). While awaiting new studies, as a precaution, a recommendation might be to not exceed ~10–15% of daily energy from ultraprocessed foods, which would correspond to a maximum of ~2 servings/d.

This change in food classification is of great interest for public health because the association with chronic diseases seems to have a greater link to the degree of processing than to the usual food groups, such as dairy, red and white meats, eggs, fruits, vegetables, legumes, and cereals (103). This has led Brazilian epidemiologists to replace usual food pyramids with technological pyramids, such as those published in the dietary guidelines for the Brazilian population (Figure 6) (104).

In conclusion, a high percentage of ultraprocessed food consumption appears to be a good holistic (nutritional) indicator, reflecting potential increased risks of chronic diseases, deterioration of animal welfare, and threats for the environment. Concerning nutrition, these products, being for the most part composed of empty calories, may also be associated with nutrient deficiencies, high glycemic index, and poor satiety potential. In other words, ultraprocessed foods represent “the tip of the iceberg,” hiding other threats to animal and environmental biodiversity. Therefore, a decrease in their consumption may well reflect an improvement in these 3 dimensions of life—that is, humans, animals, and the environment.

**Rule 3: among non-ultraprocessed foods, eat diversified, preferably local, organic and seasonal foods**

“Within unprocessed, little or normally processed foods, one should diversify by privileging organic, seasonal and local foods whenever possible.”

It is not sufficient to advise “Eat diversified”; we should add “among non-ultraprocessed foods.” Indeed, because ultraprocessed foods are empty calories, to eat various ultraprocessed foods is the same as eating only a few ultraprocessed foods. This is only calories. In this way, food biodiversity is a strategy to avoid nutritional deficiencies.

Nutritional deficits have different origins depending on whether one lives in an emerging country or in a developed country. The diet in emerging countries is a monotonous diet of minimally processed foods; so little is diversified that is at stake. In these countries, populations, especially rural, have no choice but to consume cereals, albeit not very refined, but always of the same variety. Sometimes they pair this cereal with a legume, but very often, it is the same foods (e.g., sorghum with níbe bean in some parts of Africa) without diversification of other food groups (diets low in fruits, vegetables, and animal products). This dietary monotony, combined with a high consumption of phytates, which reduce the absorption of minerals (105), leads to nutritional deficits that are harmful to long-term health, such as goiter (iodine deficiency), anemia (iron deficiency), or blindness (vitamin A deficiency). In developed countries, it is the industrial diet that is too rich in ultraprocessed foods that is to blame; these foods, refined to the extreme, have lost many of their protective micronutrients, resulting in deficits of certain minerals and vitamins (48, 106, 107). As a consequence, increased consumption of high amounts of ultraprocessed foods is concomitant with increased consumption of nutritional supplements, probably to correct “empty” calories with fiber and micro- and phytouutrients, such as in the United States (108) but also now increasingly in France (68). However, their protective effects have not been truly shown, as discussed previously (34, 35).

If focusing on the degree of food processing by encouraging people to limit ultraprocessed foods is essential to fight against the development of chronic diseases of industrialization, food biodiversity is essential to fight against nutritional deficits. Several nutritional studies in humans...
have shown that dietary biodiversity is beneficial to the body for certain functions. We report here 2 studies that are very telling. The first is an interventional study carried out in healthy women. It showed that, at equal energy intake, a meal based on 18 botanical families led to a better antioxidant status than a meal based on 5 botanical families (109). The authors concluded that botanical diversity plays a role in the bioactivity of a diet rich in fruits and vegetables and that small amounts of a myriad of phytonutrients are more beneficial to health than large quantities of a small number of phytonutrients. In the second study, which was cross-sectional, the researchers focused on cognitive abilities. They observed that people whose consumption of plant products was highly diversified had a significantly improved cognitive status compared with those whose diet was not very diversified (110). The authors concluded that the variety, not the total amount, of fruits and vegetables provides cognitive protection in adults.

The beneficial effects of food biodiversity on health can be explained by mechanisms of nutrient synergy, complementation, and/or additivity. Variety takes precedence over quantity because protective phytonutrients act in synergy: the whole is greater than the sum of the parts (42). The existence of a synergistic effect suggests natural interactions between constituents whose effect is beneficial to health. This is the illustration of the famous adage “Unity is strength” (i.e., united individuals exhibit more force than the sum of the forces of these same individuals taken in isolation). In addition, when you break up the food or isolate the constituents of their matrix, you destroy those interactions. For example, a mixture of rutin, p-coumaric acid, abscisic acid, ascorbic acid, and sugar solution was significantly more antioxidant in nature than the sum of their components (111).

This brings us to the concept of “food packages.” Our research has led us to focus, in particular, on the “packages” of antioxidants and lipotropes in cereal products (37–39). In the wheat grain, there are > 34 antioxidant compounds (38), and it is very likely that we are still far from the mark. Thus, many constituents of the same food can contribute to the same function in the body but according to different mechanisms. For example, in wheat grain, polyphenols can trap free radicals limiting their bioreactivity, some trace elements can act as essential cofactors of antioxidant enzymes
(e.g., manganese with the enzyme superoxide dismutase or selenium with the glutathione peroxidase), and other compounds such as vitamin E can stop oxidation reactions in the lipid membranes of the body's cells (112). Similarly, one and the same constituent can have several protective functions within the human body, what we call multifunctionality (Figure 7). For example, it has been shown that ferulic acid, one of the major polyphenols of wheat, can be antioxidant, acting on cell signaling, anti-diabetic, anti-inflammatory, anticarcinogenic, anti-apoptotic, hepatoprotective, neuroprotective, hypotensive, and even antiatherogenic, depending on the doses used (113). In addition, we can extend for all of the bioactive compounds of all foods. This dual complexity linked to multifunctionality and synergy of action strongly suggests minimizing the current process of refining, fractionating, and recombing foods and then enriching them at high doses with supposedly bioactive compounds that are isolated from their initial matrix.

In addition, it is important to note that the quality can also differ between the same foods based on how they are grown (for plants) or raised (for animals). Concerning organic agriculture, plant-based foods have generally better nutritional densities, notably in antioxidants, and cows pastured on grass, compared with cows raised on soy and cereal cakes, produce a milk richer in conjugated linoleic acid and omega-3 FAs (114).

How to apply these rules

We are aware of the difficulty in applying these 3 golden rules, particularly with respect to the economic challenges of eating local, organic, and seasonal foods. However, “difficult” does not mean “impossible.” We think this could be achieved at 3 levels: 1) informing the consumer, 2) educating children to consume preventive and holistic diets, and 3) favoring the access to cheap, healthy, and minimally processed foods. In addition, the agro-food industry is able to develop less-processed foods (e.g., pasta with legumes or vegetables) (115) or by using less drastic processing to reach the same shelf life for minimally processed foods than for ultraprocessed foods (e.g., high-pressure and pulsed electric fields) (116).

Concerning local aspects of organic and seasonal foods, it is highly likely that reaching 100% is not desirable or fully realistic. In a recent review, Coelho et al. (117) concluded the following: “we need more data that can provide information on the environmental, economical and health impacts resulting from the consumption of locally produced food compared to those produced far from the place of consumption [...] However, in general, the consumption of local foods, produced in ways adapted to the local environment and the use of technologies with ecological conditions, is certainly one positive factor in promoting improvements to the health of the environment, the economy and society in general.”

Interestingly, it has also been observed in the United States that the greater the number of smaller local food retail outlets in a location, the lower the rate of obesity and diabetes in that location (118). Thus, as suggested above, increasing the availability and affordability of healthy foods appear to be key strategies to improving diet and health (119). Furthermore, in a recent study, Schmitt et al. (120) associated the local and intermediary products with aspects of care and links to the territory, such as biodiversity, animal welfare, governance, or resilience, and concluded that “distance is not the most critical factor in improving sustainability of food products, and that other criteria of localness (identity, governance or size) play a more critical role.”

To conclude, it is likely that a good balance of seasonal foods, between local and global foods and between organic and conventional foods should be found to address nutritional challenges and issues. Indeed, consuming 100% local in some world regions would probably threaten the life of populations (e.g., in some desert areas).

Toward the Regionalization of Healthy Diets

We have defined the 3 golden rules for a healthy, ethical, and sustainable diet. What is interesting is that these 3 golden rules are generic enough to be applied by almost everyone on the planet regardless of the environment, except perhaps by some populations such as the Inuit of the North American Arctic, who are accustomed to a predominantly meat-based diet.

Considering the example of France, if Southern populations can easily adhere to the Mediterranean diet, the culinary traditions that are very different in the North, West and East require consideration. In the North, many potatoes are traditionally eaten, in the West more seafood is consumed, and in mountainous areas more cheeses are consumed, etc. Furthermore, climatic and agronomic conditions are also very different, whether in terms of rainfall, temperature, or soil quality.

The concept of a “regionally healthy and sustainable diet” implies developing healthy diets consistent with all dimensions of sustainability. For example, the French Auvergne region ranks first at the national level for the production of beef. Auvergne also has a large number of sheep. Vegetable production occupies one-fifth of the useful agricultural surface, the wheat being the most cultivated cereal. The region is also known for its cheese and lentil production. Can we define a sustainable healthy diet from these characteristics? The answer is certainly yes. Adopting a healthy and sustainable diet in Auvergne means acquiring supplies preferentially from local producers, within short distances, and consuming as much as possible from seasonal plant products. It may also mean reducing beef production in favor of more crops such as legumes or fruits and vegetables that are compatible with the Auvergne climate. However, it is not to say that we cannot consume nonlocal foods such as tropical fruits, coffee, tea, and chocolate, but the truth is we should probably rebalance the ratio of international to local foods in a more sustainable way.

Then, on a food basis consisting of grains and seeds, each can diversify his or her diet taking into account preferences, traditions, beliefs, economic conditions, sensitivity to animal welfare, culture, religion, etc., while trying to adhere as much
Several constituents may contribute to the same function:

- More than 34 antioxidants
- Synergy
- ↓ Oxidative stress (involved in more than 100 pathologies)

One component may contribute to several physiological functions:

- Fibers
- Multi functionality
- Transit
- Satiety
- Glycemic response
- Short chain fatty acid production
- Microbiota

**FIGURE 7** The double complexity of the food health potential: synergy and multifunctionality. Reproduced from reference 75 with permission.

as possible to the 3 golden rules. This would represent a relevant synthesis of scientific results and regional realities while combining local and international foods.

**Conclusions and Perspectives**

Nutrition is a holistic scientific discipline, in essence, that can be supplemented by reductionist studies—for example, to understand the metabolic fate of nutrients. In addition, we should operate with \( \geq 4 \) paradigm shifts to improve preventive nutrition and human nutrition research, as follows:

1. Provide more space to holism and think from holism to reductionism. We must begin with global thinking and, second, carry out reductionist studies when necessary that serve the initial holistic question in a virtuous circle.
2. Adopt a new food classification on the basis of their degree of transformation for epidemiologic studies. This challenge has already been noted by Monteiro and his colleagues (the founders of the NOVA classification) (45) and new studies are underway.
3. Do not restrict the health potential of foods to only their nutritional composition (quantitative and reductionist aspects) but include the characteristics of the physical structure of the matrix (qualitative and holistic aspects). It is only at this price that we can effectively combat the growing development of industrial diseases.
4. Define the need for more targeted primary preventive nutrition, as opposed to the actual prominent curative nutrition deriving from unhealthy foods and diets.

In addition to reductionism, holism is now essential if we are to reconcile humankind with its environment (including animals and nature), health, and diets. This will involve a significant change in the way we think. This will require us to completely reconsider how we conduct studies in the nutrition sciences. It is a huge but exciting challenge that we are facing if we are to develop sustainable diets by 2050.

We have entered a new food or nutritional transition, so we need to move toward less-processed foods and more plant-based products. Buying food is an essential act for everyone because we are all interconnected: therefore, if we buy an ultraprocessed food of animal origin containing ingredients from all over the world, we may contribute to the impoverishment of peasants in developing countries, to animal maltreatment, and to deforestation of certain parts of the world. It is up to us to choose; we are responsible, and it is now possible to have access to nutritional information and to sustainable foods in supermarkets worldwide. It is only at this price that we can advance in the right direction, for us, the animals, and the planet as a whole. Why do sustainable diets based on grains and seeds remain niche diets in our Western countries when promoting a sustainable food system is possible directly from foods sold in our supermarkets?

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