



Nutritional Ecology and Human Health

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- 4.1 Introduction – 40**
- 4.2 “Nutrition” and “Ecology” – 40**
 - 4.2.1 Human Nutrition – 40
 - 4.2.2 Ecology and Anthropology – 41
 - 4.2.3 Nutritional Ecology and Human Health – 41
- 4.3 The Importance of Appetite – 41**
 - 4.3.1 Multiple Appetites – 42
 - 4.3.2 Appetites Interact – 42
- 4.4 From Concepts to Models: Introduction to the Geometric Framework for Nutrition – 43**
 - 4.4.1 Model Selection – 43
 - 4.4.2 Selecting an Intake Target: Nutritionally Balanced and Complementary Foods – 44
 - 4.4.3 Negotiating a Compromise: When the Intake Target Cannot Be Reached – 44
- 4.5 The Geometry of Nutrition in Humans: Protein Leverage – 45**
 - 4.5.1 Do Humans Select an Intake Target? – 45
 - 4.5.2 What Is the P:NPE Rule of Compromise in Humans? – 46
- 4.6 Beyond Appetites – 47**
 - 4.6.1 The Geometry of Mixtures: Three Components in Two Dimensions – 47
 - 4.6.2 A Hierarchy of Mixtures – 47
 - 4.6.3 Dietary Macronutrient Balance – 48
 - 4.6.4 Relationships Between Macronutrient Balance and Energy Intake – 49
 - 4.6.5 Energy Balance – 49
 - 4.6.6 Beyond Energy: Protein Intake – 50
 - 4.6.7 Interactions of Appetite with the Food Environment – 51
- 4.7 Conclusions – 52**
- References – 53**

4.1 Introduction

Barely a year into the United Nations Decade of Action on Nutrition, the global community of researchers and practitioners in nutrition and associated fields has its work cut out. Malnutrition, which includes overnutrition, undernutrition, and imbalanced nutrition, affects at least a third of the earth's population and is by far the greatest contributor to the global burden of disease [1]. For the period 2014–2016, it is estimated that more than 794 million people (10.9% of the world population [2]) were undernourished and concurrently 2.1 billion were overweight or obese [3]. Both overweight and underweight are significantly associated with premature death [4], as are many other diet-related factors including excess sodium intake and micronutrient deficiencies [5]. Every year, more than 3 million children die of causes related to undernutrition [6], and in 2010 alone, overweight conditions and obesity are estimated to have resulted in 3.4 million deaths [3].

To appreciate the scale of these statistics, consider that the 3.4 million deaths attributed to overweight and obesity in 2010 is 1432 times the number of airline fatalities in the worst-ever year of commercial aviation disasters (1972) and 42 times the *total* number in 74 years of commercial aviation history [7]. It is equivalent to 6800 jumbo jets fully laden with 500 passengers each – 18 jets for every day of the year. Adding childhood deaths due to undernutrition, and we are staring in the face of what amounts to 12,800 fatal jumbo jet crashes a year, or 35 daily. Aviation-related losses would not be allowed to reach a small fraction of these numbers; in fact, since 1978 they have steadily decreased, notwithstanding the steep increase in the numbers of flights [7].

A question that is increasingly attracting attention is why have we not done a better job of preventing illness and deaths due to malnutrition? There are many views, but four themes repeatedly emerge. First, nutritional behavior and its causes and consequences are highly complex [8, 9], and the dominant models of nutrition research and practice do not pay sufficient respect to its complexity [10–12]. Second, nutrition is an intrinsically interdisciplinary problem requiring expertise from many areas – e.g., chemistry, physiology, and psychology to economics, law, and politics – but insufficient attention is paid to this fact in the training of nutrition scientists. Third, a systems perspective is needed to bring together the diverse parts of the complex multifaceted nutrition system and to identify how they interact to determine the important outcomes. Finally, we need to evolve a food and nutrition system that respects optimization goals beyond minimum cost and maximum pleasure and profit, including human health, equity, and planetary sustainability. Considerably less well-developed than the articulation of where we have gone wrong in nutrition are concrete suggestions for how we can implement a systems-based interdisciplinary agenda in nutrition science and practice to put the problem right.

In this chapter, we introduce a field from the natural sciences, called nutritional ecology, which we believe can con-

tribute toward bridging the gap between the food and nutrition system that we currently have and the system we would prefer. We begin by clarifying how we use the term “nutritional ecology” to place it in the context of related approaches. We then discuss some biological insights from nutritional ecology that we think can make a significant contribution to nutrition research and practice and thereafter introduce a geometric framework for implementing this theory. We end with examples showing how the implementation of biological thinking via nutritional geometry can provide a concrete step toward a fresh, systems-based, view of human nutrition.

4.2 “Nutrition” and “Ecology”

An important first step is to define what is meant by the term “nutritional ecology” as used in the ecological sciences (and this chapter) and how it relates to the use of the same term and the closely related term “nutrition ecology” in human nutrition.

4.2.1 Human Nutrition

In human nutrition, the first published use of either term of which we are aware was in a collection of essays titled *The Feeding Web: Issues in Nutritional Ecology* [13], which examined the impacts on health and ecological sustainability of the industrialization of the US and global food systems. Elaborating on this approach, the term “nutrition ecology” was introduced in 1986, referring to an “interdisciplinary scientific discipline that incorporates the entire food chain as well as its interactions with health, the environment, society, and the economy” where the food chain encompasses “production, harvesting, preservation, storage, transport, processing, packaging, trade, distribution, preparation, composition, and consumption of foods, as well as disposal of waste materials along the food path” [14]. Nutrition ecology is considered a new nutrition science [15], which differs from conventional human nutrition science in two key respects. Firstly, it takes a broader view that extends beyond nutritional biology to encompass also societal and ecological issues. Secondly, it emphasizes interdisciplinary systems science as a framework for dealing with the broad scope of the subject [16].

Nutrition ecology is considered to also be distinct from the field of “nutritional ecology” that has developed in the ecological sciences and anthropology [16]. We are, however, unaware of any explicit discussions on the similarities and differences between the nutritional ecology frameworks in these fields. Since “nutritional ecology” sensu the ecological sciences has recently come to focus on humans [12, 17], as the closely related framework in anthropology has done for some time now (see below), it is worth briefly examining how this term is used in those two fields.

4.2.2 Ecology and Anthropology

An early use of the term “nutritional ecology” is Schneider (1967) [18]. While based in the clinical and public health-related field of nutritional immunology [19], this prescient paper advocates the use of experimental designs in epidemiology derived from “an analysis of the problem in ecological concepts that goes beyond classical concepts in the fields of nutrition and microbiology” [18]. As we discuss below, this adumbrated a central defining feature of the ecological field of nutritional ecology, namely, the importance of applying ecological and evolutionary theory to understand the nutritional biology of animals [20].

The earliest use of the word term “nutritional ecology” that we could locate in the ecological literature is a treatise on grasshopper ecology, published in a 1962 volume of the *Memoirs of the Indian Museum* [21]. Relevant subsequent uses include Von Goldschmidt-Rothschild and Lüps (1976) [22] and Stanley Price (1978) [23]. The subjects of these publications could not have been more different from the context in which Gussow (1978) [13] used the term in relation to industrialized human environments. The study of Von Goldschmidt-Rothschild and Lüps (1976), for example, examined the extent to which domestic cats in Switzerland prey on small game birds, by dissecting the gut contents of 257 cats that had been shot while hunting [22]. Stanley Price’s study assessed the nutritional status of wild hartebeest [23]. As in Von Goldschmidt-Rothschild and Lüps’ cat study, Price did this by dissecting out the gut contents of shot animals but went further by measuring the nutritional composition of the eaten foods. He also performed digestion trials that compared the nutrient content of food eaten by captive hartebeest and sheep with the nutrient content of the feces they produced. Given how disparate Stanley Price’s study is from Gussow’s book, which appeared in the same year, it is not surprising that these works did not refer to each other, and neither did Gussow refer to any of the earlier ecological studies nor Schneider’s (1967) paper [13, 18, 23]. This suggests that the term “nutritional ecology” was probably derived independently in nutritional immunology, human nutrition, and ecology.

Over subsequent years, “nutritional ecology” became established as a subfield of ecology in its own right, being applied across animals in general, including insects [24], mammals [25], birds [26], and fish [27], as well as plants [28]. Nutritional ecology in this sense has been defined as “the science of relating an animal to its environment via nutritional interactions” [29]. These interactions involve behavioral and physiological aspects of food and nutrient acquisition and their relationship to the health, growth, and reproduction of animals [30]. A strong emphasis is on the ways that individuals adapt to nutrition-related aspects of the environment, which takes place across various timescales from short-term homeostatic responses to environmental changes, through developmental adaptation and Darwinian adaptation by natural selection [31].

The term “nutritional ecology” has been used in anthropology in much the same way that it developed in ecological sciences [32]. Jenike (2001) defined it as “...the interaction of diet, somatic maintenance, physical activity, and pathogenic agents as they relate to growth, body composition, development, and function in a constraining social, political and natural environment” [32]. This definition was modified by Hockett and Haws (2003), who defined the approach as “...the study of the relationship between essential nutrient intake and its effects on overall human health, including growth and maintenance in individuals and general demographic trends in populations” [33]. Both definitions share, in common with the ecological sciences, an emphasis on the individual within the context of the environment.

4.2.3 Nutritional Ecology and Human Health

The origins of nutrition ecology (in human nutrition) and nutritional ecology (in the ecological sciences and anthropology) thus differed, with the former being focused more on the broader human nutrition system and the latter on the individual within that system. In the terms of ecological science, this broadly reflects the difference between the sub-fields of community ecology (emphasis on community-level issues, such as food webs) and functional ecology (emphasis on the characteristics of individuals that adapt them to their environments) [34]. This difference is not, however, absolute, but more an issue of emphasis. Nutrition ecologists do not exclusively consider the social and environmental dimensions of nutrition, but also the biological dimension [15]. Likewise, nutritional ecologists are aware of the importance of the biological characteristics of individual organisms in shaping the ecological communities within which they exist [20, 35]. Issues of emphasis are, nonetheless, important because they influence the questions, theory, and methods that direct progress in a scientific field.

In the remainder of this chapter, we demonstrate using our own work how the biological theory and methods from nutritional ecology can provide new insight into human nutrition and its links to health [12]. The perspective that we bring derives from almost three decades of research into the nutritional ecology of non-human organisms, ranging from slime molds, yeast, and insects in laboratory studies to giant pandas, monkeys, gorillas, and orangutans in the wild [36]. We do not view this approach to be an alternative to nutrition ecology, but rather a means to expand human nutrition science to integrate the interests and expertise of nutrition ecology with the biological theory and the comparative perspective of nutritional ecology.

4.3 The Importance of Appetite

Among the most emphatic messages to emerge from our studies of non-human animals is that appetite is paramount for understanding foraging, feeding, and its impacts on the

animal and, ultimately, on the community of which it is a part. This might seem obvious, except that biological theory combined with studies on the nutritional ecology of non-human animals has provided a more nuanced and powerful concept of appetite than currently exists in human nutrition science.

In this section, we summarize the biological background to the nutritional ecology view of appetite and, in the following section, introduce an approach for modeling and measuring appetite in this sense. Thereafter, we show how these models can help to integrate appetite within the broader human nutrition system to help bridge the gap between the biological theory and methods of nutritional ecologists and the integrative goals of nutrition ecology [15].

4

4.3.1 Multiple Appetites

To appreciate the subtleties of appetite, we need to step back and ask the question “what is appetite for?” This is a good stage to point out that the “what for?” question is a hallmark of the evolutionary framework on which nutritional ecology is based; it aims to understand biological traits partly through knowledge of what they evolved to achieve [37]. The power of this approach is that it provides an expectation of, firstly, how the biological trait should be designed to achieve its evolved function and, secondly, how it should respond in various circumstances. For example, it can help to understand how the human appetite works and how it might respond to the industrialized food environments of which Gussow (1978) wrote in the book that first used the term “nutritional ecology” in the context of human nutrition [13].

The simple answer to the question “what is appetite for” is that it evolved as a “control center” that directs the animal to meet its nutritional needs, in the same way that thirst directs it to drink and the sensation of cold causes shivering and heat-seeking behavior. To achieve its purpose, however, appetite should be considerably more complex than motivations such as thirst or temperature-related discomfort, for several reasons. First, thirst and temperature regulation have simple endpoints (sufficient hydration and optimal temperature, respectively), whereas an animal’s nutrient needs are complex, involving many nutrients, each required at its own particular level. Second, the relative needs for different nutrients change over time and with the circumstances of the animal; for example, female birds have elevated protein and calcium requirements for producing eggs [38], whereas more fat and carbohydrates are needed to fuel the costs of long-distance migration [39]. Meeting multiple and changing nutritional needs in this way, in complex and changing environmental circumstances, is a substantial challenge.

An animal could not deal with this challenge if it had only a single appetite that, for example, caused a bird to eat the same diet regardless of whether reproducing or preparing for migration, any more than we would expect a motor car to have only a single warning light that did not distinguish between an oil and gasoline shortage. Theory therefore

predicts that animals should have separate appetites for specific nutrients to help ensure that they eat the specific blend of nutrients that is appropriate for their particular needs at a given time. Such “nutrient-specific appetites” are known to exist for many animals, including humans (see ► Sect. 4.5). Although the details of which nutrients are regulated by specific appetites are expected to differ with the ecological and evolutionary circumstances of different species, the universal importance of the macronutrients protein, carbohydrates, and fat means that most animals have separate appetites to regulate either two or all three of these [36]. Some also have specific appetites for the minerals calcium [40] and sodium [41].

4.3.2 Appetites Interact

Important as they are, the possession of nutrient-specific appetites is not on its own sufficient to ensure that animals satisfy their nutrient needs [42]. An added complexity is that most nutrients are not available separately in the environment, but come packaged in mixtures called foods. If a food contains the same ratio of different nutrients as is needed by the animal – for example, high protein relative to carbohydrate and fat when reproducing – then the complex nature of foods is a benefit, because this enables the animal to satisfy its requirements for all nutrients from one source. It is, however, seldom the case that the composition of foods exactly matches the mix of nutrients needed, and this complicates nutrition considerably, both for animals and for attempts by nutritional ecologists to understand animal nutrition.

Where possible, animals deal with this challenge through “complementary feeding,” in which specific combinations of nutritionally imbalanced foods are mixed in the right proportions to balance the diet overall. This requires that the appetites for the different nutrients cooperate to ensure that each is eaten at a level that meets, but does not exceed, the respective requirements. Many animals have been shown to balance their diets in this way, both in laboratory experiments and in the wild [36], and so too do humans (see ► Sect. 4.5.1).

In reality, however, ecology is not always so obliging as to provide combinations of complementary foods that can be mixed to obtain a balanced diet. Rather, animals often find themselves in situations where the only foods available restrict them to eating a diet that is imbalanced with respect to their nutrient needs. For example, many primates that need both fruits, which are high in sugars and fats, and protein-rich leaves to balance their diet, endure periods of fruit scarcity in which they are forced to eat a leaf-rich diet containing excess protein [43].

In this situation, the appetites for protein and non-protein energy enter into conflict, because the target intakes for both cannot be achieved simultaneously. Rather, the nutritional options available to the animal are to eat the target level of protein and suffer a shortage of non-protein energy, to eat the target level of non-protein energy while overeating protein,

or to settle on an intermediate outcome in which it has both a moderate excess of protein and a moderate shortage of non-protein energy. Research has shown that different species resolve this competition between appetites in different ways, which likely reflect the relative costs of under- or over-eating the two nutrients [36].

While such interactions between appetite systems are complex, they are also extremely important for understanding how diet influences the behavior, the physiology, and the health of animals. To help simplify the challenge, we have invented a modeling approach called the Geometric Framework for Nutrition (GFN). In the following section, we introduce the basic concepts of GFN and show how they have been applied to understand macronutrient regulation in humans.

4.4 From Concepts to Models: Introduction to the Geometric Framework for Nutrition

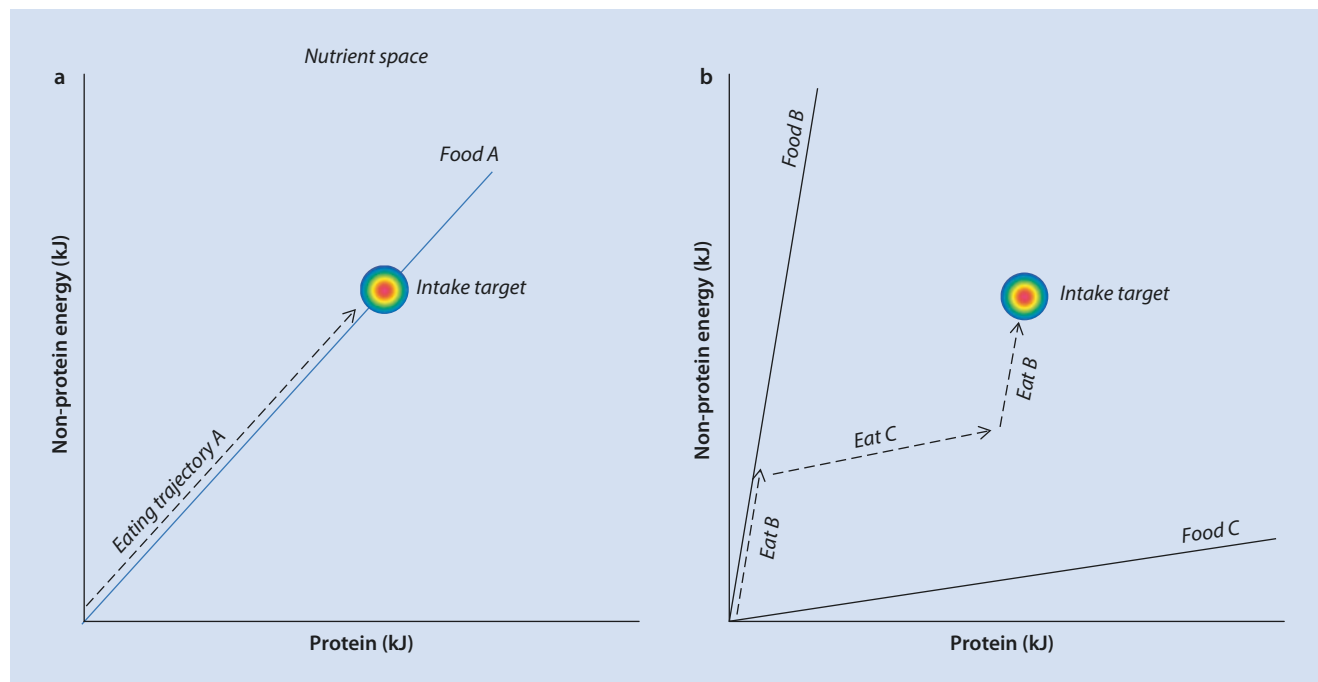
The value of the ecology- and evolution-inspired concepts from nutritional ecology is substantially enhanced if these concepts can be expressed in quantitative models. Quantitative models provide a framework within which the various relevant factors can be measured and their relation-

ships explored to interpret the ways in which they interact to influence important outcomes such as energy intake and health [44]. We now demonstrate how the nutritional ecology ideas from the previous section can be modeled using the simple geometry of GFN (■ Fig. 4.1). Thereafter, we show how these models have been applied to understand macronutrient regulation and its consequences for energy intake in humans.

4.4.1 Model Selection

The first step in constructing a GFN model is to select the nutrients that are relevant to the problem under investigation. In so doing, special care should be taken to heed the dictum attributed to Einstein that “things should be as simple as possible ... but no simpler”: we should include in the model only those nutrients that we suspect play an important role in the problem, but ensure that all of the nutrients that do so are included. A common problem in human nutrition science is the tendency to attribute outcomes such as obesity to individual nutrients, usually fats or carbohydrates, without regard for how they interact with other nutrients in exerting their influence [12, 45] (please see ► Chap. 8).

Since our example concerns obesity, we will focus on the energetic macronutrients protein, fat, and digestible carbo-



■ Fig. 4.1 Basic concepts in the Geometric Framework for Nutrition. The “nutrient space” is the space formed by the two nutrient axes, in this hypothetical model protein (horizontal) and combined fats and digestible carbohydrates (non-protein energy) [vertical]. An “intake target” is plotted within the nutrient space, representing the amount and balance of nutrients (in this case protein and non-protein energy) that are targeted by the animal’s regulatory systems. Foods are represented as lines, called “nutritional rails,” which originate at the origin and project into the graph at angles that represent the ratio of

the nutrients that each contains. As the animal eats, it ingests the nutrients in the same ratio as they are present in the food it is eating, and its nutritional state thus changes along a trajectory identical to the rail for that food. The animal can therefore reach its intake target either by selecting a food that has the same ratio of nutrients as the intake target (i.e., a nutritionally balanced food) (food A, in a) or by switching between foods that are individually imbalanced but together nutritionally complementary (foods B and C in b)

hydrates, although in different contexts we might be interested in other nutrients (e.g., [46]). We will also initially simplify the model by combining fats and carbohydrates into a single category to address the question of how the human appetite for protein (P) interacts with non-protein energy (henceforth NPE) to drive energy intake (■ Fig. 4.1). Our reasons for doing this are that, firstly, in some contexts, fats and carbohydrates can be regarded as interchangeable sources of metabolic energy for humans [47] and, secondly, as we show in the next section, when all three macronutrients are considered in their own right, distinguishing fats and carbohydrates in the data that we present as an example does not provide a better explanation for energy eaten than does considering them combined. We note, however, that in many other contexts – for example, appetite interactions in mice [48] and the causes of cardiovascular disease in humans [49] – it is important to distinguish fats and carbohydrates and even the different sub-categories of these nutrients. Geometric models can readily be applied in this context.

Having selected the nutrients of interest, the next step is to make a graph where each nutrient is represented on its own axis, as shown in ■ Fig. 4.1. Here, too, there is an important decision to make, regarding the units in which to represent the different nutrients – for example, whether mass (grams) or energy (kilojoules). In our model, we have chosen energy units, because the aim is to understand how different blends of macronutrients influence energy intake.

We have now constructed a *nutrient space*, which provides the platform on which we model how the appetites for different macronutrients interact to influence energy intake (■ Fig. 4.1).

4.4.2 Selecting an Intake Target: Nutritionally Balanced and Complementary Foods

An important reference point in modeling appetite interactions is the *intake target*, or the point in nutrient space that shows the amounts and balance of the nutrients that the appetite systems will target under circumstances in which they are unconstrained by the quality or quantity of available food (■ Fig. 4.1). Theory predicts, and studies have shown, that in many cases the selected intake target provides a diet that optimally satisfies the animal's needs for the different nutrients [50–52]. The animal is able to reach its intake target through the appetites for the different nutrients working in harmony to meet the respective intakes that are best for the animal.

The way that the animal satisfies its nutrient needs is, of course, by eating foods, but the important question is *which* foods the animal can eat to reach its intake target. To examine this, we can plot in the model the composition of various foods, as lines called *nutritional rails*, which project from the origin into the nutrient space at an angle determined by the ratio of the nutrients that each contains. As the animal eats, it ingests the nutrients in the same ratio as is contained in the

food it is eating. Its nutritional state can therefore be viewed as “moving” through the nutrient space at an angle equivalent to the rail for the food it is eating and over a distance determined by how much of the food it eats. ■ Figure 4.1a shows that food A contains the same ratio of the nutrients as does the intake target (the rail passes through the intake target), and in the spatial metaphor of the model, the animal can therefore “navigate” to the target by eating this food (feeding trajectory A in the figure). This food is thus *nutritionally balanced* with respect to the animal's requirements for protein and non-protein energy.

Foods B and C, by contrast, do not pass through the intake target – they are *nutritionally imbalanced* with respect to P and NPE (■ Fig. 4.1b). However, since food C contains too much P relative to NPE (falls to the right of the target) and food B too much NPE relative to P (to the left of the target), the two foods are *nutritionally complementary* and can be combined in appropriate proportions to provide a balanced diet. Complementary feeding is shown in the nutrient space as a zigzag trajectory, where each leg represents an amount eaten of the respective foods (■ Fig. 4.1b).

4.4.3 Negotiating a Compromise: When the Intake Target Cannot Be Reached

Animals can therefore reach their intake target by selecting balanced foods (e.g., ■ Fig. 4.1a) or mixing their intake from nutritionally complementary foods (■ Fig. 4.1b). What options does the animal have when confined to a single nutritionally imbalanced food or non-complementary combination of imbalanced foods? As discussed above, in this case the target point cannot be reached for both nutrients, and the appetite systems need to negotiate a compromise that minimizes the cost to the animal of its dietary predicament. Such strategies are known as *rules of compromise*.

A distinguishing feature of GFN is that it enables us to model the various rules of compromise and thereby to understand the strategies that animals have evolved to deal with dietary imbalance. ■ Figure 4.2 shows three examples, representing extreme responses chosen from a wide range of possible strategies [36, 53]. In the blue strategy, protein wins over entirely – the animal eats to the point on the nutritional rail where its need for P is met, regardless of whether NPE is under-eaten (on high P:NPE diets) or overeaten (on low P:NPE diets). This pattern, known as *protein prioritization*, has been observed in wild spider monkeys [54] and orangutans [55]. The green strategy is the opposite, namely, prioritization of non-protein energy, where P is over- or under-eaten to meet the NPE target. This pattern is shown by wild mountain gorillas, which overeat protein to obtain the target level of fats and carbohydrates in periods when fruit shortage commits these animals to a high-protein diet [56]. It is also been observed in several carnivores, including mink [57] and predatory beetles [52]. The red strategy represents the situation where neither nutrient group dominates over the other, but the appetite systems give equal weighting to

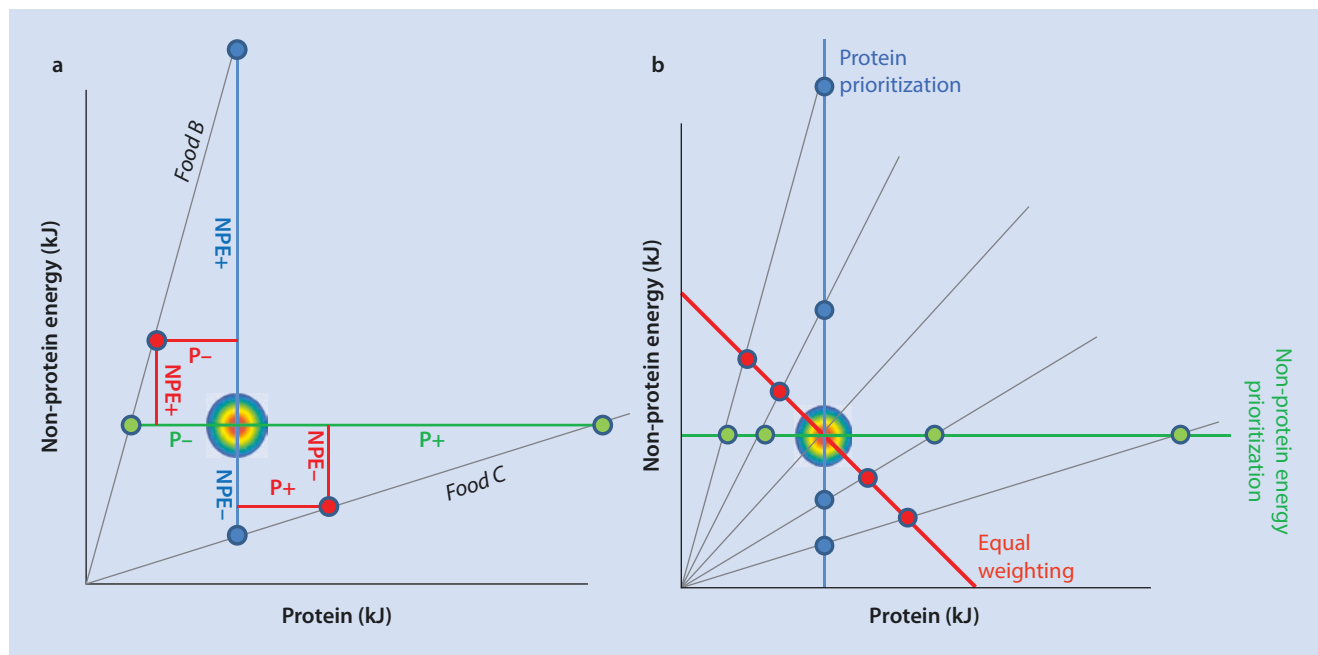


Fig. 4.2 a Schematic showing geometric representation of possible regulatory responses to nutrient imbalance. When confined to a single nutritionally imbalanced food (i.e., with a rail that doesn't intersect the intake target), the animal needs to resolve a trade-off between over-ingesting one nutrient and under-ingesting the other. By feeding to the green point, it meets its target for non-protein energy (NPE, comprising fats and carbohydrate combined) at the cost of suffering a shortage of protein of magnitude P- on low P:NPE diets (e.g., if restricted to food B) or a protein excess (P+) on high P:NPE diets (food C). The converse would be true if the animal ate to the blue points – it would meet its protein target, but to do so would have to ingest an excess or deficit of NPE (NPE+ and NPE-, respectively). By feeding to either of the red points, the animal would meet its target for neither nutrient, but would ingest a moderate excess of NPE and a defi-

cit of P on food B or a moderate excess of P and a deficit of NPE on food C. b Testing different experimental groups, each on one of a range of foods varying in nutrient balance, provides a description of how the animal resolves the trade-off between over- and under-ingesting nutrients when confined to imbalanced foods, termed a rule of compromise (ROC). Three possibilities are illustrated: the blue symbols represent absolute prioritization of protein (i.e., feeding to the target coordinate for protein regardless of whether this involves over- or under-eating NPE), the green symbols represent NPE prioritization, and the red symbols represent an intermediate response in which the regulatory systems assign equal weighting to excesses and deficits of the two nutrients (P- = NPE+ on food B and P+ = NPE- on food C). Many other configurations are possible

each: it eats to the point on the imbalanced nutritional rail where the ingested excess of one nutrient exactly matches the deficit of the other. This pattern has been observed in wild rhesus macaque monkeys [58] and several species of generalist-feeding herbivorous insects [36].

4.5 The Geometry of Nutrition in Humans: Protein Leverage

How do humans regulate macronutrient intake, and can this help to understand obesity? These questions have been addressed in several independent studies, including randomized control trials [59–61], analyses of data compiled from the literature [62], and survey data of human populations [63–65]. Results of these studies have consistently highlighted the importance of appetite interactions in driving energy intake.

4.5.1 Do Humans Select an Intake Target?

A recent study has addressed this question, with striking results. Following protocols developed by Gosby et al. (2010),

Campbell et al. (2016) presented 63 Jamaican volunteers with 3 menus from which to select a diet over 3 days within a residential experimental facility [61, 66]. All 3 menus contained the same 29 dishes, but the compositions of the dishes were manipulated using added protein and carbohydrate such that all options on one menu had 10% of energy from protein, a second had 15%, and a third had protein at 25%. Fat was held constant at 30% for all dishes and menus. Since the human diet seldom contains less than 10% protein or more than 25%, we reasoned that if an intake target exists, then it lies somewhere between these extremes and can be reached by composing a diet from the experimental menus through complementary feeding. The menu with 15% protein represented our best guess at what the composition of the target diet is, because this is close to the mean intake levels found in Western diets [67].

Results are plotted in Fig. 4.3. The three solid radial lines are nutritional rails representing the compositions of the experimental menus, and the blue-shading shows the area that could potentially be reached by subjects in this experiment. Despite the wide range of possibilities, it is striking that all subjects, whether male or female, clustered tightly around a line representing 14.7% protein, although males ate

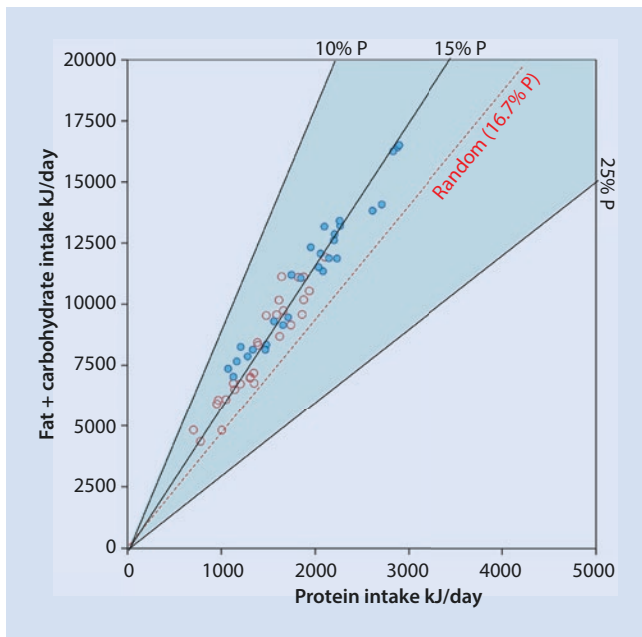


Fig. 4.3 Daily protein and non-protein energy intakes self-selected by 63 adult Jamaican volunteers, averaged for each subject over the 3-day experimental period. Red symbols are females, and blue symbols are males. The solid radial lines are nutritional rails representing the compositions of the three experimental menus from which the diets could be freely selected (10, 15, and 25% protein by energy). The pale blue region represents the range of diets that could theoretically be selected from these menus, and the dotted red line represents the expected outcome if the subjects mixed the diets randomly (16.7% P). The data show that subjects selected a diet of 14.7% protein, which was significantly different from the random outcome. (Adapted from Campbell et al. [61]. With permission from Creative Commons License)

more of the diet overall than females, which is not surprising given their larger body size.

One possible explanation for this pattern is that the subjects did not distinguish between the three diets based on their macronutrient content, but simply ate equal amounts of each. It can be calculated that if this were the case, the intake points would align along the dashed radial line, representing a diet with 16.7% protein. However, the actual intakes differed with a high degree of statistical certainty from this line, showing that they represent macronutrient regulation to a P:NPE intake target. An earlier experiment by Simpson et al. (2003) showed similar results [68].

4.5.2 What Is the P:NPE Rule of Compromise in Humans?

Several studies, including randomized control trials [59, 60, 68], analyses of experimental data compiled from the literature [62], and observational studies using diet surveys [63], have addressed the question of how humans respond to macronutrient-imbalanced diets. Since the results all tell the same story, we will present only the data of the literature compilation of Gosby et al. (2013), as expanded by Raubenheimer et al. (2015) [62, 69].

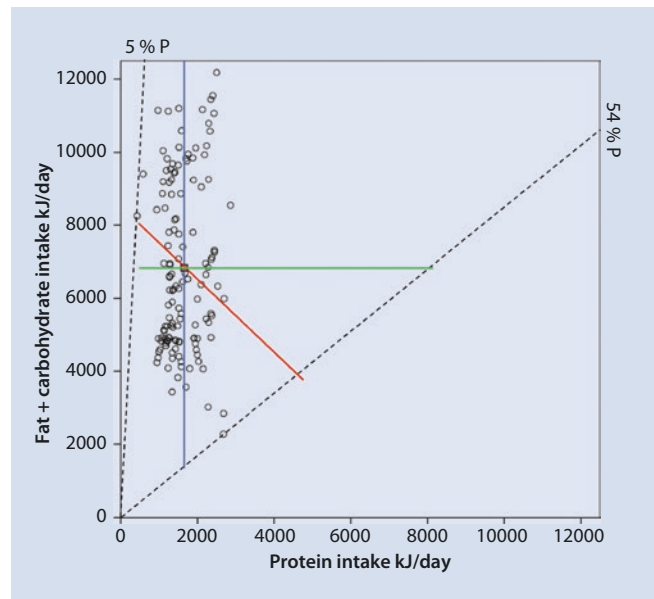


Fig. 4.4 Interaction of human appetite systems with dietary macronutrient ratios. Data are protein (x-axis) and non-protein (fat + carbohydrate, y-axis) ad libitum energy intakes by subjects restricted to 1 of 138 experimental diets [62, 69]. The black dashed radials represent the nutritional rails for the diets with the highest (54%) and lowest (5%) proportional protein content. The area between these radials is the region of the nutrient space within which points for nutrient intakes are constrained to lie, with the pattern of actual intakes being determined by the ways that appetites for protein, fat, and carbohydrate interact. The blue, red, and green lines represent the protein prioritization, NPE prioritization, and equal weighting models from Fig. 4.2. The analysis shows that humans maintain absolute protein intake relatively tightly, with non-protein energy intake varying more passively with dietary macronutrient ratios. (Adapted from Raubenheimer and Simpson [12]. With permission from Annual Reviews)

What all of these studies in the compilation have in common is that each experimental subject was restricted to one of a range of single diets, each with fixed P:NPE ratio, and allowed to eat as much of their respective diet as they wished. The experiments therefore test how the human appetite systems interact to determine protein, fat, and carbohydrate intake as dietary macronutrient balance varies – i.e., the rule of compromise for these nutrients. The result is shown in Fig. 4.4. Protein intake remained relatively stable over a wide range of diet compositions, while the intake of fats and carbohydrates increased with decreasing dietary P:NPE ratio. Humans thus show the protein prioritization pattern of macronutrient regulation (Fig. 4.2).

This analysis shows that information about the dynamics of human appetite systems is essential for understanding why we eat the amounts of nutrients and energy that we do. The main conclusion that it presents is by no means obvious: it suggests that humans will overeat fats and carbohydrates not because they have a particularly strong drive to eat these nutrients, but because of a strong appetite for *protein*. On the other hand, we should not interpret this to suggest that the human appetite is exclusively about protein. We know that this is not the case, because when allowed to select a diet from nutritionally complementary foods, humans regulate

the intake of both P and NPE (■ Fig. 4.3). Rather, in circumstances where it is possible, the appetites for different macronutrients cooperate to select a balanced diet, but when limits on available foods prevent this, protein regulation overrides and fat and carbohydrate intakes follow more passively.

This phenomenon, where the appetite for protein influences the intake of other nutrients such as fats and carbohydrates, has been termed *protein leverage* [47].

4.6 Beyond Appetites

Our discussion to this point illustrates the logical progression of research within the nutritional ecology framework. We began by showing that evolutionary and ecological reasoning predicts that animals should have separate appetites for different nutrients and that these appetite systems should interact to determine nutrient intakes. We then introduced nutritional geometry as an approach for measuring such appetite interactions and demonstrated how it has been applied to humans. Results showed that the humans in our study selected an intake target of approximately 15% energy from protein, and when restricted to macronutrient-imbalanced diets that prevented them from achieving this target, they showed the protein prioritization rule of compromise, in which fats and carbohydrates are passively over- or under-eaten as the percentage of dietary protein varies.

This is, principally, an examination of organismal (in this case human) biology, which, as we commented above, is an important starting point for nutritional ecology research. The next step is to expand the model to understand how the trait, in this case appetite interactions, engages with broader aspects of the animal's nutritional biology, including specific nutrient requirements and the food environment that nutrition ecologists have emphasized in their writing.

One hypothesis that addresses this is the *protein leverage hypothesis* (PLH) [47]. PLH proposes that the protein prioritization pattern of macronutrient regulation has interacted with reductions in the P:NPE ratio of the human diet to drive fat and carbohydrate overconsumption and obesity. This hypothesis can potentially provide a powerful bridge between human biology, modern human environments, and health because, if true, it simplifies the search for the causes of the obesity epidemic. It does this by focusing attention on a very simple question about the role of environmental change in driving this epidemic: *what is the cause of protein dilution in the human diet that leads our appetite systems to overeat fats and carbohydrates?*

Simple questions are not, however, necessarily simple to answer, and this is no exception. Like human biology, modern industrialized human food environments are extremely complex, and the interactions between human biology and modern environments potentially all the more so. To help deal with this complexity, we have adopted from nutritional ecology a form of nutritional geometry called the right-angled mixture triangle (RMT); [70]) (■ Fig. 4.5). In the remainder of this chapter, we introduce the RMT and dem-

onstrate in the context of the protein leverage hypothesis how it can provide an aid for understanding the biology-environment interactions that influence health in industrialized food environments.

4.6.1 The Geometry of Mixtures: Three Components in Two Dimensions

As its name implies, the RMT is an approach for modeling mixtures. The axes are therefore scaled as the proportional (or %) contribution of each nutrient to the overall mixture, rather than absolute amounts, as is the case in the GFN models of appetite interactions (e.g., kilojoules eaten per day, as in ■ Figs. 4.3 and 4.4). The key difference between these two variants of nutritional geometry is thus that one is proportions-based and the other is amounts-based. Beyond that, they share much in common and are, in fact, complementary approaches for modeling nutrition.

As is the case for amounts-based geometric models, the first step in building an RMT model is to decide which nutrients are most relevant to the problem. Since we are extending the analysis of how macronutrient appetites interact to influence energy intake, we will include in our model the macronutrients protein, fats, and carbohydrates expressed in energy units. An important advantage of the RMT approach, however, is that it enables all three nutrients to be modeled in a simple two-dimensional graph. Amounts-based geometry can also cope with more than two nutrients, but generally only by simplifying the model (e.g., combining two nutrients into a single axis, as for fats and carbohydrates in ■ Figs. 4.3 and 4.4) or else by plotting three two-dimensional graphs (protein vs. fat, protein vs. carbohydrates, and fat vs. carbohydrates).

To illustrate how three components are represented in a two-dimensional RMT, consider the black point in ■ Fig. 4.5a, representing the macronutrient composition of a sample of rice. The percentage contribution of protein to total macronutrient energy in the rice is 5% (x-axis) and of fat is 10% (y-axis). Since % protein + % fat + % carbohydrate must add up to 100% of macronutrient energy, it is easy to see that % carbohydrate = $100 - (\% \text{protein} + \% \text{fat}) = 100 - (5 + 10) = 85$. Geometrically, 85% carbohydrate is represented by a diagonal line that connects the same value on the x- and y-axes and intersects the point representing the sample of rice. Any mixture of macronutrients that comprises 85% of energy from carbohydrates will fall on this line, which is plotted in the figure as the black dotted diagonal labeled “85.”

By the same logic, it can be seen at a glance that the peas in the plot comprise 25% of energy from protein, 5% from fat, and 70% from carbohydrate, and the steak comprises 40% protein, 60% fat, and 0% carbohydrate.

4.6.2 A Hierarchy of Mixtures

Just as the macronutrients combine in specific proportions in foods, so too do foods combine into meals, meals into diets,

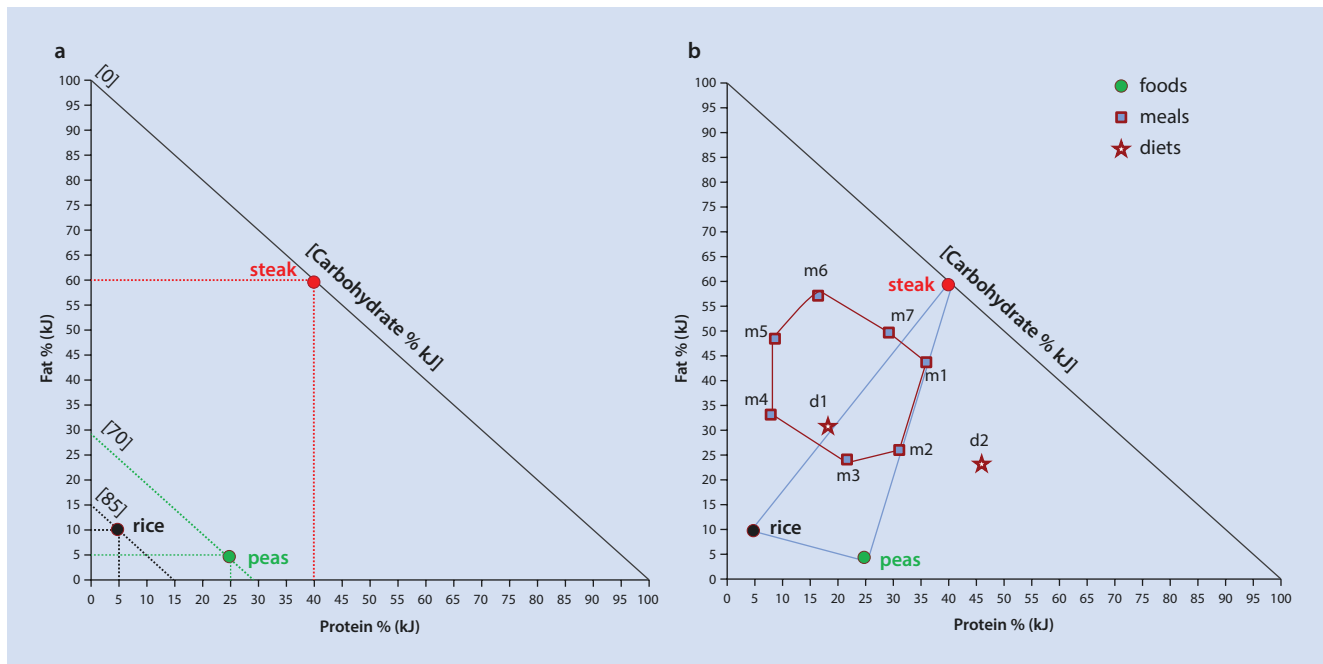


Fig. 4.5 **a** Right-angled mixture triangle [70] illustrating how components (in this case the macronutrients) combine into foods (rice, peas, and steak). Points represent the percentage contributed by each component (protein, fat, and carbohydrate) to the sum of the three. Thus, the macronutrient composition of rice is 5% protein and 10% fat, and since protein, fat, and carbohydrate sum to 100%, carbohydrate = $100 - (5 + 10) = 85\%$. This value is represented by the negative dashed diagonal joining 15% on the x- and y-axes, such that any mixture of macronutrients containing 85% of carbohydrate will fall on that line. Likewise, the peas contain 25% protein, 5% fat, and 70% carbohydrate, and the steak

contains 40% protein, 60% fat, and 0% carbohydrate. **b** Foods combine into meals (m1–m7), and meals combine into diets (d1 and d2). A meal composed of two foods (e.g., peas and steak) is constrained to fall on the line connecting those foods (e.g., m1 and m2), with the exact position along the line being determined by the proportion of the foods in the meal. Adding a third food (e.g., rice) expands the set of possibilities to a triangle (meals m1, m2, and m3 can be composed from the three foods, but m4–m7 cannot). By extension, diets d1 can be composed from meals m1 to m7, but d2 cannot. (Adapted from Raubenheimer and Simpson [12]. With permission from Annual Reviews)

and diets into dietary patterns. Recent work in nutritional ecology has emphasized the value of considering all of these levels for understanding the nutritional strategies of animals [71]. This is critically important in human nutrition, because each level in the hierarchy engages in different ways with the complex organism-environment interface of humans in industrialized food environments [12].

For example, nutrients, the base level in the mixture hierarchy, interact with physiology, by engaging taste receptors, appetites systems, and numerous physiological pathways relevant to health (e.g., the insulin signaling system). It is not, however, nutrients that we buy, but principally foods, and to understand our shopping choices, we need to consider also this level in the hierarchy. Although some foods are eaten directly, the greatest portion of the human diet is eaten as mixtures of foods, called meals. Meals, therefore, are important levels of focus for understanding human eating choices. And yet neither foods nor meals are the primary link between nutrition and health; for that we need to consider the long-term cumulative intakes of foods and meals, namely, diets. To close the circle, diets impact health and disease principally via their primary components, the nutrients.

A powerful aspect of RMT plots is that they can model all levels in this hierarchy of mixtures, as illustrated in Fig. 4.5b. Consider, for example, a meal comprised of two foods, peas and steak. The macronutrient composition of this meal is con-

strained to fall on the line connecting these foods, with the exact position determined by the proportions of the two foods in the meals. Thus, meal compositions labeled m1 and m2 are attainable from peas and steak, but m3–m7 are not. If additional foods are included in the diet, then the set of possible meal compositions expands to a space. For example, a meal consisting of peas, steak, and rice can take on any macronutrient composition that falls within the triangle formed by these foods (e.g., m3), but no composition that falls outside of the triangle (m4–m7). By the same logic, meal m1–m7 could combine into a weekly diet that falls within the polygon formed by connecting these meals (e.g., d1), but not outside of it (d2).

4.6.3 Dietary Macronutrient Balance

Distinguishing and interrelating different levels of the dietary mixture hierarchy in this way provides important benefits for examining the ways that human nutritional biology engages with industrialized food environments. However, to realize the potential of this approach, we need to move beyond describing mixtures such as foods, meals, and diets and examine how they link to human biology and to the food environments with which our biology interacts. An important first step is to relate these compositional data to nutrient requirements.

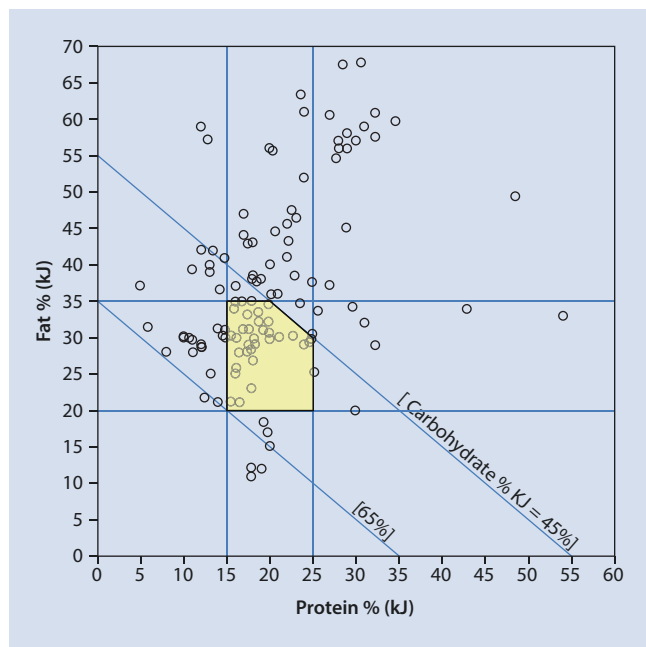


Fig. 4.6 Macronutrient compositions of the 138 experimentally fixed diets plotted from **Fig. 4.4**. The yellow polygon is an integrated representation of Australian/New Zealand Acceptable Macronutrient Distribution Range (AMDR; %P = 15–25%, %F = 20–35%, %C = 45–65%), such that diet points falling within this polygon represent macronutrient-balanced diets and those falling outside are macronutrient-imbalanced. (Adapted from Raubenheimer and Simpson [12]. With permission from Annual Reviews)

To illustrate, **Fig. 4.6** presents in RMT format the same data as plotted in **Fig. 4.4**, representing the compositions of experimental diets compiled from the literature. As the figure shows, the data spanned a wide range of protein–fat–carbohydrate mixtures. To examine how these mixtures relate to proportional macronutrient requirements, we used for reference the Acceptable Macronutrient Distribution Ranges (AMDR) for Australia and New Zealand [72]. According to these recommendations, 15–25% of energy intake should come from protein, 20–35% from fat, and 45–65% from carbohydrate.

Delineating these individual ranges in **Fig. 4.6** enables us to identify the region representing diets that satisfy all three recommendations, plotted as yellow polygon. Any diet with a composition that falls within the yellow region is thus macronutrient-balanced with respect to the AMDR, and any diet that falls outside is macronutrient-imbalanced.

4.6.4 Relationships Between Macronutrient Balance and Energy Intake

Central to the protein leverage hypothesis is the question of how energy intakes relate to dietary macronutrient ratios. We already have shown that low dietary protein leverages the intake of excess fat and carbohydrate and now address the implications for total energy intake. To do this, in **Fig. 4.7**, we have constructed a response surface onto the data from **Fig. 4.6** that relates the ad libitum energy intakes (which

was a voluntary response of the subjects) to macronutrient ratios of the diet (the experimentally fixed variable) [69].

The analysis shows that total energy intakes increased (intake values grade from blue to red) as the percentage of energy contributed to the diet by protein decreased (movement from right to left on the protein axis). This result substantiates the protein leverage effect shown in **Fig. 4.4**, but takes it further. First, it shows that the leveraging by protein of fat and carbohydrate intake (**Fig. 4.4**) translates into increased total energy consumption, as predicted by the protein leverage hypothesis. Second, energy intake changed as dietary protein varied (along the x-axis), but remained relatively constant along the fat axis. This suggests that, for these data at least, the main determinant of energy intake was the protein energy ratio (x-axis), with little effect of the relative proportion of fat:carbohydrate, and justifies our decision, discussed above, to combine fat and carbohydrate into a single axis (**Fig. 4.4**). Finally, plotting the data in this way helps to integrate additional factors into the model, such as energy balance.

4.6.5 Energy Balance

An important reference point for predicting the effects of protein leverage on obesity is Equilibrium Energy Intake (EEI), or the point at which energy intake matches energy expenditure. Energy intakes that exceed EEI signify positive energy balance and risk of fat accumulation, while lower intakes signify negative energy balance.

To incorporate the concept of energy balance into the model relating macronutrient ratios to energy intake, we estimated the EEI (given body size, sex, and expected activity levels under the experimental conditions) for the subjects from the experiments represented in the analysis to be 8813 kJ/day [69]. This value can be incorporated into the model as an EEI contour, represented in **Fig. 4.7a** as the bold dashed line. Intakes to the left of this line represent positive energy balance, and intakes to the right represent negative energy balance.

We can now relate across the experimental population dietary macronutrient balance (position in relation to the AMDR polygon) to energy intakes and energy balance, to predict the compositions of diets that will cause human appetites to drive energy overconsumption. An interesting feature of the model is that the EEI contour passes through the AMDR region. Assuming the same applies more generally within the relevant populations, this suggests that following the official New Zealand and Australian recommendations for proportional macronutrient intakes would spontaneously lead to balanced energy intake.

For comparison, we have also plotted in **Fig. 4.7a** the US AMDR [73]. The recommendations for carbohydrate and fat are the same as the Australian and the New Zealand AMDR, but the range for protein is broader, spanning 10–35% of energy intake. The model suggests that following the low end of the protein range (10–15% of energy intake from protein) would lead to energy overconsumption and

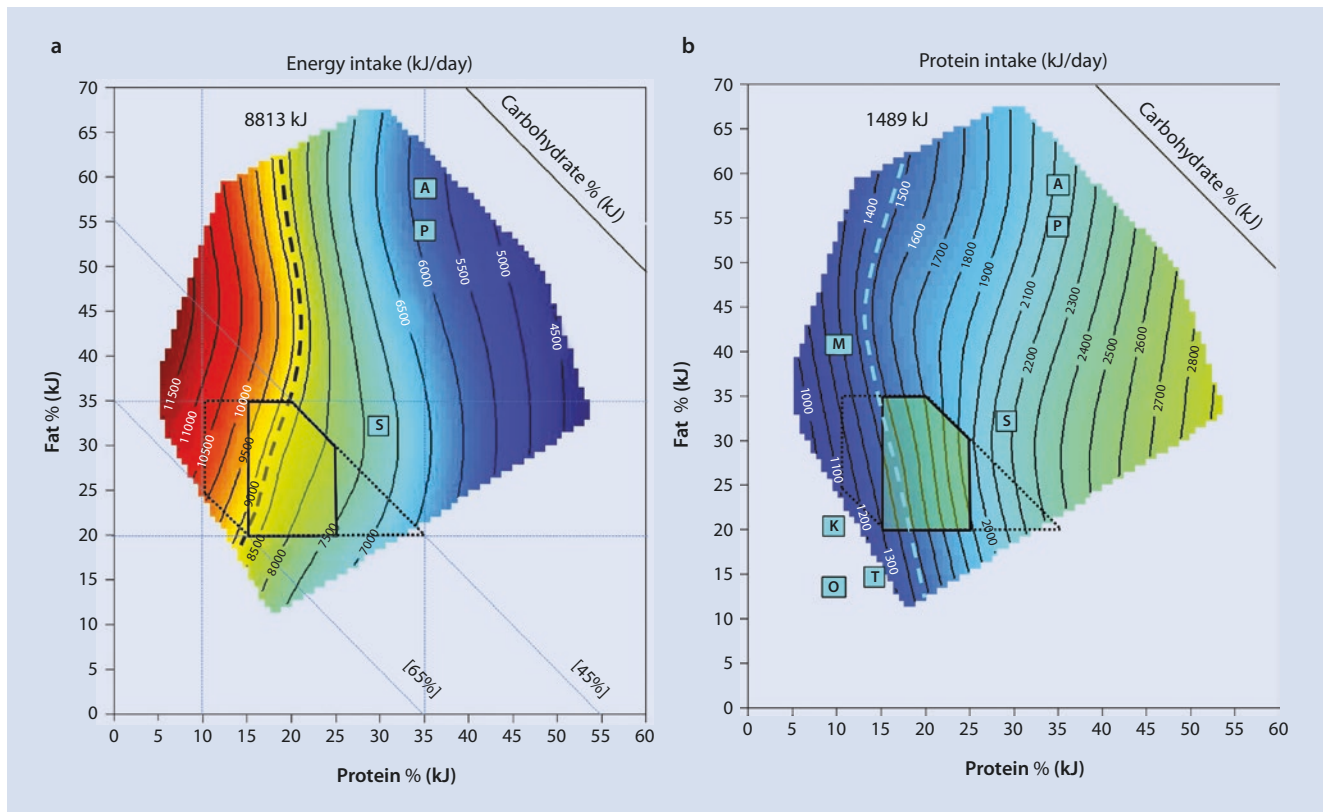


Fig. 4.7 **a** Response surface showing ad libitum daily energy intakes associated with the experimental diet compositions plotted in **Figs. 4.4** and **4.6**. The dashed contour represents estimated equilibrium energy requirements (8813 kJ) for sex and weight assuming a physical activity level (PAL) of 1.5, which is commensurate with activity levels in the experimental subjects. The data suggest that energy equilibrium was achieved on diets with 15–20% protein, with energy balance being negative and positive for diets with higher and lower % protein, respectively. The model is consistent with the association between weight loss and high-protein diets, such as the Atkins (A), Protein Power (P), and Sugar Busters (S) diets: their macronutrient compositions fall within the blue region of low ad libitum energy intakes. The dotted polygon represents the AMDR for the USA, which has the same ranges for fat and carbohydrate as the

Australia/New Zealand AMDR, but a wider protein range (spanning 10–35%). **b** Response surface showing ad libitum protein intakes associated with the data in **a**. The dashed contour represents approximate average protein requirements for the study population (1489 kJ). The figure shows that protein intakes considerably higher than estimated requirements are associated with diets having macronutrient compositions equivalent to high-protein weight loss diets (A Atkins, P Protein Power, and S Sugar Busters). Conversely, low protein intakes are likely to be associated with the macronutrient composition of the diets associated with exceptionally healthy and long-lived human populations, the Mediterranean (M), Kitavan Islander (K), Tsimane (T), and traditional Okinawan (O) diets. (Adapted from Raubenheimer et al. [69]. With permission from The Obesity Society)

positive energy balance. In contrast, the high end of the US range for protein (25–35%) corresponds with low energy intakes and negative energy balance (the blue region). Indeed, the protein leverage effect can help to explain why many popular high-protein weight loss diets including the Atkins, Paleo, and Sugar Busters, which are shown in the figure, fall within this region.

4.6.6 Beyond Energy: Protein Intake

While the above analysis suggests a reason based on human appetite interactions (protein leverage) why high-protein diets are effective for weight loss (in the short term at least), we caution that low energy intake is not the only effect of consuming diets with high protein energy ratios. Another outcome is that compensation for the low levels of fats and

carbohydrates results in protein overconsumption, albeit to a smaller extent than low protein leads to fat and carbohydrate overconsumption [12].

To illustrate, in **Fig. 4.7b** we have plotted the corresponding protein intake surface for the data shown in **Figs. 4.6** and **4.7a**. We have also calculated the Estimated Average Protein Requirements for the subjects in the experimental trials to be 1489 kJ and plotted this as a contour equivalent to the EEI contour in **Fig. 4.7a**. Viewing the data in this way clearly shows the increase in absolute protein intakes with increasing dietary % protein (left to right on the x-axis). It also shows that estimated dietary protein requirements are met for diets with approximately 15–20% protein energy, and at higher dietary protein densities, excess protein is ingested.

There is now strong evidence that excess protein intakes are associated with negative cardiometabolic profiles and accelerated aging, especially when coupled with low carbo-

hydrate intakes [45, 74]. Consistent with this is the observation that the healthiest dietary patterns, including the Mediterranean, traditional Okinawan [75], Kitavan Islanders [76], and Tsimane [77] diets, are associated with low dietary protein densities and low protein intakes, as shown in Fig. 4.7b. This should caution against high-protein diets, such as the Atkins, high-protein Paleo, and Sugar Busters diets (Fig. 4.7), except as therapeutic interventions for weight loss. It also raises questions about the high end of the protein range sanctioned by the US AMDR.

In comparing Fig. 4.7a, b, the alert reader might have noted an apparent inconsistency. The Mediterranean, Kitavan Islander, traditional Okinawan, and Tsimane diets all have low protein energy ratios (between 10% and 15%) (Fig. 4.7b) and under the model presented in Fig. 4.7a should thus be associated with excess energy intake, and yet obesity is not a problem within these societies. The reason for this apparent inconsistency is that the parameters of such models, including the shape of the surface relating energy consumption-to-macronutrient ratios, are population-specific and might be influenced by differences in nutrient and other aspects of the respective food environments. For example, the low-protein dietary patterns in Fig. 4.7b are associated with high fiber content compared with Westernized diets to which the model in Fig. 4.7a applies. High fiber is likely to induce satiety [78] at lower levels of protein (and energy) intakes than are low fiber diets [69], as has been demonstrated in mice [45]. The combination of low protein and high fiber thus has the double health benefits of limiting protein intake while avoiding energy overconsumption. The extension to consider also fiber emphasizes the importance of matching the model to the context and also demonstrates how these models can be built incrementally to incorporate multiple food constituents. Equally important is their extension to include broader components of the food environment, beyond diet composition.

4.6.7 Interactions of Appetite with the Food Environment

To this point we have built a model that integrates human appetite interactions with a range of factors relevant to the relationships between diet and health, including the nutrient-food-meal-diet mixture hierarchy, dietary macronutrient ratios, intakes of energy and protein, recommended dietary macronutrient proportions and protein intakes, and energy balance. The model demonstrates one advantage of doing this: it helps to identify how these factors interrelate to explain the links between diet, health and disease.

Another advantage of building such a model is that it provides a context for identifying important aspects of our food environment that might influence the relationships within the model. For example, among the most salient and influential aspects of industrialized food environments is economics, giving rise to the question of whether the cost of foods might play a role in influencing the macronutrient composi-

tion of our diets. To address this, Brooks et al. (2010) calculated the relationship between the concentration (g/100 g) of protein, fats, and carbohydrates and the cost (in US dollars/100 g) of 106 supermarket foods [79]. Results showed that the cost of supermarket foods is positively related to their protein content (Fig. 4.8). This suggests that economic considerations might be one factor that contributes toward diluting dietary protein content in industrialized food environments, an influence that our model has shown is transduced via the protein leverage effect into increased energy intake. In this way, protein leverage might help to explain the well-established association between lower socioeconomic status and obesity [80].

We might likewise address the question of why the USDA AMDR spans such a wide range of dietary protein densities, encompassing both low-protein diets (10–15% protein), which our model suggests are likely to be associated with excess energy intake (Fig. 4.7a), and the high end (25–35%), associated with excess protein intake and premature aging (Fig. 4.7b). One possibility is that this reflects influence on research and government policy by the food industry, rather than health considerations. For example, the sugar and affiliated industries selectively sponsor research that casts doubt on recommended upper limits to sugar intake, and the meat, dairy, and egg industries do the same for protein [81, 82]. These industries also exert influence on dietary guidelines through political lobbying [82].

Several other possible facets of industrialized food environments that might interact with human appetite systems to influence health have been identified. These include the influx of low-protein processed foods into the human food

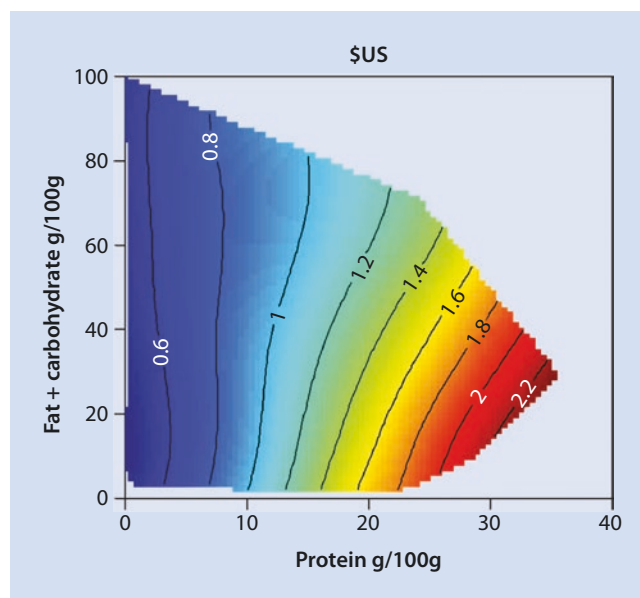


Fig. 4.8 Relationship between the concentration (g/100 g) of macronutrients (protein, fat, and non-structural carbohydrates) and the cost (\$US/100 g) of 106 supermarket foods. Cost increases from dark blue to red. The graph suggests that the cost of food increases with protein density but is unaffected by fat and carbohydrates. (Reprinted with permission from Raubenheimer et al. [17])

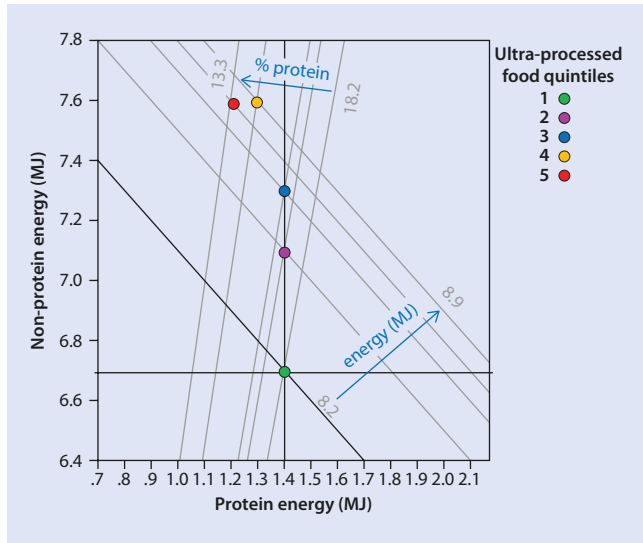


Fig. 4.9 Relationship between ultra-processed food consumption and protein leverage. The symbols represent protein and non-protein energy intakes for the lowest (green) to highest (red) quintiles of ultra-processed food (UPF) consumption reported in the National Health and Nutrition Examination Survey 2009–2010. The negatively sloped diagonals represent daily total energy intakes (calculated as the sum of $X + Y$), and the positive radials represent the dietary protein:non-protein energy ratio (X/Y). The dark vertical, horizontal, and diagonal lines represent alternative models to explain the data, as in **Fig. 4.2** and **4.4**. The data show that increased inclusion of UPF in the diet corresponds with reduced dietary protein density (18.3–13.3%) and increased total energy intake (8.2–8.9 MJ), as predicted by the protein leverage hypothesis. (Reprinted with permission from Martinez Steele et al. [64])

supply (**Fig. 4.9**) [64] and the reduction in plant protein that may be associated with rising atmospheric carbon dioxide [17], both of which could potentially have the effect of diluting the energy contribution of protein, thereby increasing energy intake.

In addition to such influences on the compositions of foods and diets, another interesting possibility is that environmental factors might interact directly with human biology to influence the parameters of protein leverage. For example, any factor that reduces protein efficiency could exacerbate protein leverage, by increasing the intake target of the protein appetite, thus requiring a stronger compensatory response to protein dilution (**Fig. 4.10**) [47]. Such environment-induced variation in protein leverage might explain a number of poorly understood correlations between obesity and environmental factors. One example is the association of obesity with recent cultural transitions from traditional high-protein diets to Westernized diets rich in fats, oils, and simple carbohydrates [47]; another is the vulnerability to later-life obesity of infants fed high-protein milk formulas [17]. In both cases, high-protein diets are hypothesized to developmentally program low-protein efficiency, thus exacerbating protein leverage (**Fig. 4.10**).

We cite these examples to illustrate how an understanding of the dynamics of human appetite systems might help to illuminate the factors that have driven the epidemic of obe-

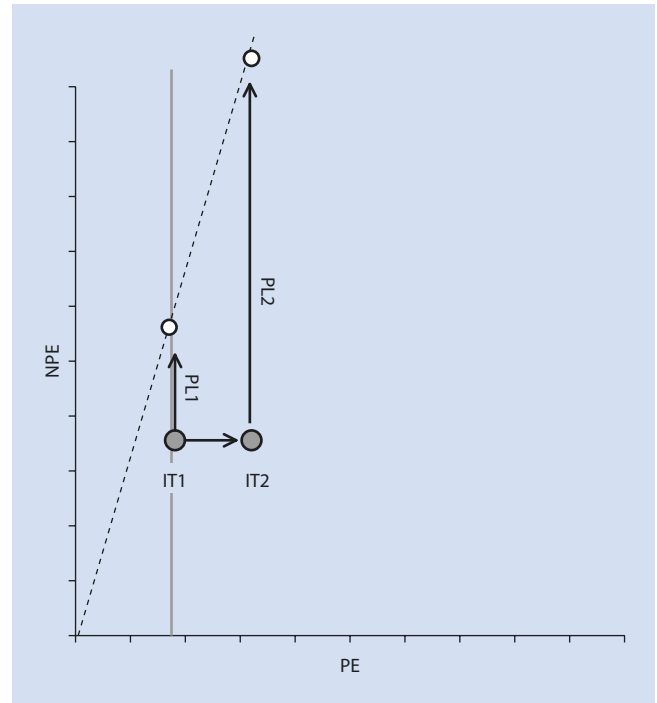


Fig. 4.10 Schematic showing the effect on protein leverage of an increase in the protein coordinate of the intake target, as might come about through decreased protein efficiency. The x-axis represents protein energy (PE) and the y-axis energy from carbohydrates and fat (NPE). The dashed radial shows the macronutrient composition of a food that has a lower PE:NPE ratio than intake target IT1. The arrow labeled PL1 denotes the extent to which surplus intake of carbohydrate and fat is leveraged by the mismatch between the PE:NPE ratio of the food relative to target IT1. For the same food, protein leverage is greatly exacerbated (PL2) for a small change in the protein coordinate of the intake target (IT1 increases to IT2). (Reprinted with permission from Raubenheimer et al. [17])

sity and associated disease in recent decades. The broader message, however, is that a nutritional ecology perspective, which emphasizes the interaction between biological traits and food environments, can provide a structured research framework for generating and testing hypotheses regarding the causes of health and disease in our radically altered industrialized food environments.

4.7 Conclusions

Statistics such as those with which we opened this chapter leave no doubt that nutrition science ought to be doing a better job of preventing premature deaths that are associated with malnutrition and chronic disease. The challenge, however, is to understand how the diverse and complex set of interacting causes drives the problem and to identify the key control points that are amenable to intervention to improve nutrition-related health. There is now widespread recognition that success will require a systems-based approach, which recognizes that relevant causal components are distributed across and between domains representing diverse academic disciplines and societal sectors [8–12, 83]. The

leadership, however, must come from nutrition science, which at present is ill-equipped for the task.

We have suggested in this chapter that a constructive branch for interdisciplinary engagement is with the basic biological sciences. Although nutrition science clearly has drawn heavily on chemistry, molecular biology, and physiology, its engagement with the core theory of biology – evolutionary and ecological theory – has been rudimentary. Such theory can provide a powerful framework for identifying pivotal systems components and interactions, and in this way direct and simplify the task, in much the same way that aerodynamics theory can help to direct aviation research. Ecology and evolution also provide a broad comparative perspective, which helps to identify patterns and generalities across a wide range of species and environments and, in this way, enrich the understanding of human-environment interactions. Nutritional ecology is the branch of the natural sciences that applies this approach in the context of nutrition.

As an example, we have shown how biological theory predicts that separate appetites would exist for particular nutrients and that these appetites would interact to broker beneficial outcomes across the range of varied food environments within which they evolved. We introduced nutritional geometry as an approach for investigating appetite interactions and examining how they are linked to broader aspects of human biology and industrialized food environments. Our analysis suggests, somewhat counter-intuitively, that the human propensity to overeat fats and carbohydrates is closely linked to our appetite for protein, via protein leverage. This, in turn, suggests a different focus for examining the causes of obesity, through drawing attention to the factors that influence dietary protein density. Our analysis also cautions against the common tendency to assume that if “too little is bad, a lot must be good,” by highlighting the dangers both of diets with too low and too high protein energy density. It emphasizes the importance of dietary *balance*.

In closing, we emphasize that our main goal is not to suggest that we have solved the problem of energy overconsumption, obesity, and related diseases, but rather to introduce a biologically inspired approach that can help to structure nutrition research. Beyond the macronutrients and their different types and constituents, other dietary components such as fiber and micronutrients clearly are relevant to the problem, and likewise, many nutrient combinations are important for various other aspects of health. We suggest, however, that these relationships are best examined in a framework that is guided by biological theory and which examines the interactions among nutrients rather than considering them separately.

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