Who's Afraid of Nutritionism?

Jonathan Sholl and David Raubenheimer

Various scientists and philosophers have heavily criticized what they see as problematic forms of 'nutritional reductionism' or 'nutritionism' whereby studying food–health interactions at the level of isolated food components produces largely misguided science and misleading interpretations. However, the exact target of these diverse criticisms remains elusive, and its implications are overstated, which may hinder scientific understanding. To better identify the types of flaws supposedly hindering reductionist research, we disentangle three types of reductionist claims to better determine what the debate is about and to propose ways to move it forward. We then present a qualified defence of the reductionist programme that hinges on the ability to identify nutritional causes that make a difference, which we illustrate through central examples in the history of nutrition. This defence is taken further by using insights from the philosophy of mechanisms to analyse how the field of nutritional ecology offers a synthetic framework to explain, generate, and test predictions about nutrient–organism interactions, which is premised on the biological mechanisms of nutrient-specific appetite regulation. The result, which we call 'synthetic reductionism', avoids many, though perhaps not all, of the challenges raised by anti-reductionists, and also highlights the potential of reductionism to identify nutritional difference makers.

1. Introduction

As the study of nutrition became an established scientific domain in the early-twentieth century, one of its key aims has been to dissect the seemingly endless complexity of food–health interactions (Carpenter [2003a], [2003b], [2003c], [2003d]). Arguably, the central method has been to study these interactions on increasingly fine-grained levels whereby specific nutrients and other food components are isolated and identified to better determine what it is in foods and diets that impacts human health (Mozaffarian et al. [2018]). While this has advanced our general understanding, many scientists and philosophers question whether these 'reductionist' methods have outrun their apparent utility. More specifically, they suggest that this aim to isolate nutrient-health effects has come at the expense of food and dietary level research and is now a hindrance to be transcended (Hoffmann [2003]), producing largely misguided science and misleading or even harmful interpretations. Anti-reductionist sentiments, most of which posit that foods or dietary patterns should be the fundamental explanatory levels, abound in nutrition research (Messina et al. [2001]; Zeisel et al. [2001]; Hoffmann [2003]; Jacobs and Tapsell [2008]; Fardet and Rock [2014], [2018], [2020]; Mayne et al. [2016]; Mozaffarian et al. [2018]; Rees [2019]; Moughan [2020]; Spector and Gardner [2020]; Campbell [2021]; Temple

[2023]). Recently, philosophers have begun echoing the accusation that such reductionism or 'nutritionism' (Scrinis [2008], [2012], [2013]) is the dominant nutritional ideology (Siipi [2013]; Borghini et al. [2021]).

Before proceeding, it is important to stress the significance of these concerns as they reflect broader changes in nutrition research, policy, and public understanding. Nutrient reductionism is sometimes viewed as a problem so pervasive that it demands an 'alternative' framework with which to explain and interpret food–health interactions (Jacobs and Tapsell [2008]; Scrinis [2013]; Fardet and Rock [2014]). This concern is closely linked with attempts to situate nutrient-level explanations within the evidential context of whole foods, food quality, or dietary patterns (Hu [2002]; Jacobs and Tapsell [2013]; Tapsell et al. [2016]), and how, in various countries, dietary guidelines are increasingly built around whole foods categories while minimizing nutrient aspects.[1] These tendencies are explicitly linked to recurring concerns about overcoming reductionism (Mozaffarian et al. [2018]), which have made their way into popular discourses about nutrition (Pollan [2007]). Given this, the rather academic question of the role of reductionism in nutrition has implications spanning philosophy, science, public health, and food policy.

Despite such growing concerns, what is meant by 'reductionism' in these various debates remains amorphous. For instance, some authors appeal to ontological aspects of foods that elude reductionist methods (Jacobs and Tapsell [2008]; Jacobs et al. [2009]), others frame the problem such that methodological reductions to food components are only useful when set within a distinct research paradigm (Tapsell et al. [2016]; Fardet and Rock [2018]; Scrinis and Monteiro [2018]), and still others highlight the seemingly insurmountable explanatory limitations of reductionist methods (Hoffmann [2003]; Temple [2023]). Each of these claims has different implications regarding the fate of reductionism for nutrition research and none are without important challenges. Building on recent interest in philosophical issues facing the nutrition sciences (Jukola [2019], [2021]; Sholl [2022]; Bourrat and Griffiths [forthcoming]), we aim to evaluate these concerns over reductionism while arguing against uncritically following the prominent forms

[1] See the website of the Food and Agricultural Organization of the UN, available at <www.fao.org/nutrition/education/food-dietary-guidelines/home/en/>; and 'Dietary Guidelines for Americans, 2020–2025' on the US Department of Agriculture and US Department of Health and Human Services website, available at <www.dietaryguidelines.gov/>.

of anti-reductionism found throughout philosophy of science (Nagel [1998]; Grantham [2004]; Rosenberg [2020]).

In this article, we seek to organize these diverse critiques of nutritional reductionism by distinguishing the problems they raise. One overarching issue concerns distinguishing between the misinterpretations and harmful implementations of nutrition science versus the claim that scientific explanations relying on reductionist methods are seriously flawed (sec. 2). While flawed science can foster misinterpretations, our concern is with how critics depict these scientific flaws. To organize these accusations, in section 3 we disentangle three types of anti-reductionist claims to better distinguish the targets being critiqued and to identify where disagreements lie. Addressing these points of disagreement, we present a qualified defence of reductionist methods in two parts. First, section 4 evaluates the epistemic aims of methodological reductions in terms of providing 'proportional' explanations (Woodward [2004]) that help identify nutritional factors that 'make a difference' (Waters [2007]). Next, building on recent philosophical research into the role of mechanisms for developing nuanced accounts of reductionist explanations (Machamer et al. [2000]; Bechtel and Richardson [2010]; Craver and Darden [2013]), section 5 analyses how the field of nutritional ecology provides a synthetic framework to explain, generate, and test predictions about nutrient–organism interactions, which is premised on the 'decomposition' of feeding behaviours into the biological mechanisms of (macro)nutrient-specific appetite regulation (Raubenheimer et al. [2015b]; Raubenheimer and Simpson [2016], [2020]). While the kind of reductionism employed in this field avoids many, though perhaps not all, of the challenges raised by anti-reductionists, identifying when reductionism can detect causally relevant nutritional factors helps avoid counter-productive reductions and guards against the misinterpretations of scientific findings that anti-reductionists decry while better capturing reductionism's explanatory potential.

Our central argument is that while these various critiques of 'reductionism' raise many valid concerns, some critiques present a narrow view of what reductionism is (or can be) and misrepresent the explanatory aims guiding robust (methodological) reductions. In doing so, this risks obscuring the utility of reductions to nutrients for not only providing mechanistic explanations of and useful predictions about food-health effects but also for enabling the integration of evidence.

2. Demarcating the Critique: Reductionism and Its Discontents

As mentioned above, one key issue singled out as plaguing the nutrition sciences is an excessive reliance on 'reductionist' methods to study and interpret food–health interactions, which some consider the 'dominant paradigm' or a 'virtually inescapable' ideology (Pollan [2007]; Jacobs and Tapsell [2008]; Scrinis [2008], [2013]). Clarifying the specifics of this critique will help determine what it is about 'reductionism' that these authors find so problematic.

One of the central figures leading these charges is philosopher and social theorist Gyorgi Scrinis. His work provides an extensive analysis of what he labels 'nutritionism' (or nutritional reductionism) and how this problematic methodology has solidified throughout the history of nutrition science, and feeds into public health and popular dietary discourse (Scrinis [2008], [2013]). Two features are at the core of his notion of nutritionism: the healthfulness of foods or diets is primarily studied and explained by focusing on nutrient composition (regardless of the food source) and these findings are then interpreted in ways that decontextualize, oversimplify, and exaggerate their health implications.[2] While he mentions various forms that this reductionism has taken throughout history (for example, quantifying, moralizing, and functional reductionism), significant attention is given to two general forms: nutrient-level and single-nutrient reductionism (Scrinis [2012]). The former consists in explaining and interpreting the health effects of foods in terms of their macronutrient constituents, such as proteins, fats, or carbohydrates, whereas the latter involves explanations and interpretations based on specific types of nutrients, such as polyunsaturated fats, fructose, vitamins, and so on. While Scrinis largely targets these two forms of reductionism, there is also 'single-food' reductionism in which one food is singled out as explaining the harms or benefits of a broader dietary pattern, for example, linking heart disease to 'egg consumption' in a Western diet (Scrinis [2013], pp. 325–27). Throughout all these examples, he targets the well-established use of reductionist methods to motivate scientific explanations and subsequent interpretations.

[2] 'Nutritionism—or nutritional reductionism—is characterized by a reductive *focus* on the nutrient composition of foods as the means for understanding their healthfulness, as well as by a reductive *interpretation* of the role of these nutrients in bodily health' (Scrinis [2013], p. 2).

While part of Scrinis's project is descriptive, the identification of nutritionism is driven by the aim to condemn it for its faults. The key problem is that the study of nutrients outside the broader dietary context (what he calls 'reductionism') is misguided and leads to narrow-minded inferences that oversimplify and decontextualize the complex interactions between foods and health. For instance, this reductionism purportedly oversimplifies the complexity of nutrient interactions, or the importance of food quality or processing types (Jacobs and Tapsell [2013]; Shao et al. [2017]; Cena and Calder [2020]); it obscures how the same nutrients produce different outcomes in the context of whole foods or dietary patterns (Maximova et al. [2020]); and subsequently nurtures adversarial debates about isolated components, such as sugars or saturated fat (or carbohydrates versus fats in general) as being uniquely harmful (Scrinis [2012]; Ludwig et al. [2018]; Mozaffarian and Forouhi [2018]; Mozaffarian et al. [2018]).

We feel it is useful to separate the critiques of problematic explanations that affect scientific research itself and the subsequent misinterpretations and misguided implementations based on this research.[3] Starting with the latter—the overly simplistic and exaggerated interpretations—we agree that there are serious problems concerning the selective use of evidence to support dietary advice and popular discourse, especially in today's social-media-heavy (Wang et al. [2019]; Diekman et al. [2023]) and epistemically polluted (Levy [2018]) informational ecology where many (non-)experts make strong claims based on isolated studies or mechanisms.[4] This can be observed in the marketing by food companies or diet proponents who narrowly focus on specific components to make tenuous or disingenuous claims about a product's or diet's healthfulness (Kroker-Lobos et al. [2022]). It is also found in public health or policy recommendations that are either too hasty in their generalizations from basic research or that fail to provide sufficient context and nuance about why (or not) to eat specific nutrients, foods, or dietary patterns (see also Folker and Sandøe [2008]). In this context, the terms 'nutritionism' or 'reductionism' are targeting multiple sociological issues generally arising downstream of scientific

[3] Mirroring concepts in the sociology of scientific knowledge (Bloor [1991]), Scrinis ([2013], pp. 14–20) argues against viewing nutritionism as a problem of when 'good science' is misused or misinterpreted, as this constitutes a weak critique; instead, his aim is to develop a strong critique of nutrition science as such. With the latter, the problem is not merely the misapplication or misinterpretation of solid science but runs deep into the historically embedded, excessive scientific focus on nutrients. While his 'strong' critique keeps the issues of explanation and interpretation closely linked, we argue that their separation can allow for more nuance.

[4] For a compelling popular discussion of this, see (Guyenet [2023]).

practice, all loosely exhibiting an implicitly or explicitly biased use of evidence. We concur that these reductive misinterpretations require serious consideration, especially as this research is often disseminated by industry-funded institutions (Nestle [2007]) or on social media platforms in ways that run counter to public health.

While reductive misinterpretations can arise due to flawed science, our focus is on how these critics depict these scientific flaws. In other words, our primary concern is with the accusations that there is something misguided about using reductionist methods to isolate food components and explain their health effects. Though Scrinis is one of the more strident critics or sceptics of reductionism (Scrinis [2020]; Scrinis and Monteiro [2022]), many similar critiques can be found in the scientific literature expressing varying degrees of dissatisfaction with the role reductionism has played, and continues to play, in nutrition research (Messina et al. [2001]; Hoffmann [2003]; Jacobs and Tapsell [2008], [2013]; Tapsell et al. [2016]; Fardet and Rock [2020]; Spector and Gardner [2020]; Campbell [2021]). For instance, we find rather strong claims that 'the reductionist approach fails to adequately describe the multiplicity of metabolic effects on the entire organism' (Hoffmann [2003]); that 'we do not have complete knowledge of food composition and some effects may result from unidentified or underappreciated components' (Jacobs et al. [2009], p. 1544S); that the effects of food-level properties on health 'cannot be fully explained on the basis of the effects of "the sum of the nutrients" alone' (Moughan [2020]); that our current 'nutrient profiling models are unable to adequately capture the physicochemical complexity of foods' (Scrinis and Monteiro [2022]); and thus that 'the relationship between diet and health can only be understood as the combined action of many different substances present in foods' (Temple [2023]). Throughout his work, Scrinis ([2012], [2013]; Scrinis and Monteiro [2018]) relies heavily on these critiques by scientists to further demonstrate that the core of most nutrition science is rotten. Many of these critiques express the intuitions that people 'eat food, not nutrients' and that food–health interactions are 'too complex' to be sufficiently explained by nutrient-level research (Jacobs and Tapsell [2008]; Tapsell et al. [2016]; Fardet and Rock [2018]; Temple [2023]). If the diagnosis is an excessive and narrow focus on nutrients, the alternative is to identify something at the level of foods and dietary patterns that better captures the complexity of food–health interactions.

Now, it is hard to deny that an excessive amount of research focuses on single nutrients, components, or other single variables, such as single food categories. For example,

recent analyses found that a large majority of systematic reviews discuss evidence pertaining to the health effects of specific nutrients, rather than focusing on foods or dietary patterns (Lawrence et al. [2016]; Bero et al. [2019]), an issue further fueled by industry funding (Fabbri et al. [2017]). There is thus a diagnosis of too much reductionism from a disproportionate amount of single component research. This becomes problematic when it fosters the view that complex health problems, or health interventions, can be boiled down to these isolated components (Simpson et al. [2015]), such as occurred with β-carotene and vitamin E (tocopherol) (Hercberg [2005]; Scrinis [2013]). It is also problematic because it seems to rest on what has been deemed 'one variable at a time' research that obscures or downplays multivariate nutrient–organism interactions (Simpson et al. [2015]). It should be noted that even attempts to focus on specific food-level properties, such as food processing, may risk reducing food–health interactions to a single variable at the expense of others (Raubenheimer and Simpson [2016]). Given this, the diagnosis is not only too much, but ineffective reductionism that suggests fraught links between one variable and some outcome.

To be clear, many of these critiques reach for middle ground by acknowledging that reductionist methods might have limited utility for studying the role of nutrients in human health. Their main concern is when these methods are employed outside the context of foods and diets, seen as exclusively explanatory, or thereby produce or contribute to misguided interpretations or interventions. However, this raises questions concerning how to delimit the scope of these diverse critiques: do they have a shared target? Is reductionism itself the problem or only specific forms of it? Similarly, while some concede a role, albeit limited, for 'less reductive' science (Scrinis [2013]; Tapsell et al. [2016]; Fardet and Rock [2018]), what exactly makes it better? Is there 'good' reductionism and how might it be identified?

3. Disentangling (Anti-)Reductionism: Where's the Debate?

Philosophers have been debating the issue of reductionism and anti-reductionism in science for decades, and they have made some useful distinctions between types of reductionism that can help organize the diverse targets in the above critiques. Utilizing the standard distinctions between ontological, methodological, and explanatory questions (Nagel [1998]; Rosenberg [2007], [2020]), we ultimately suggest that the central issue at stake involves clarifying the explanatory aims of methodological reductions.

3.1. Ontological reductionism

This first issue is about whether whole systems can be reduced to their constituent parts, with the strongest formulation being that wholes are nothing but their parts (Nagel [1998]). In the context of nutrition, one way to formulate this would be to argue that foods are (nothing but) specific components or their sum. For instance, some decry so-called exclusive reductionism or when foods are viewed as 'only the sum of nutrients' (Fardet and Rock [2020]). This strong reductionist formulation of foods as nutrient aggregates (Wimsatt [2007]) does not seem to be what is at stake in the above debates, since everyone surely agrees that foods are comprised of their constituents, be they nutrients, vitamins, or various components. In short, the starting point seems to be that foods are or contain much more than specific components, even if only some are studied at a given time.

Accordingly, the central debate seems more about how to interpret the claim that foods are 'more than' these component parts. Reformulating Nagel ([1998]), ontological anti-reductionists might claim that even if we had a complete description of all food components, there would still be something more that emerges out of the complex interactions among components and foods that cannot be accounted for with reductionist methods. This is reflected in claims that whole foods or diets contain additional 'features not found in any one of the parts' (Hoffmann [2003]), typically spelled out in terms of 'food synergies' (Jacobs et al. [2009]), the 'food matrix' (Jacobs and Tapsell [2008]; Aguilera [2019]), or in the unique interactions between these properties of whole foods and our physiology, whether studied in terms of their effects on the microbiome, oxidative stress, or other measures (Hoffmann [2003]; Fardet and Rock [2014], [2018]). These latter concepts point to the complex combinations of nutrients or foods in a diet, to structural aspects of 'whole' foods, or the irreducible effects these properties have on our health.

In themselves, these research programmes can help to identify potentially distinct causal pathways by which foods impact our physiology. However, we flag the need to guard against tendencies to overstate the implications of these pathways. For instance, this could lead to a form of 'greedy holism' (Gatherer [2010]) if it suggests that there is some irreducible or mysterious property of whole foods that is forever out of the reductionist's reach (a 'food-component-of-the-gaps' claim), 'despite any amount of data' (Fardet and Rock [2014], p. 440). Philosophers have proposed that emergent and top-

down causal properties can still be compatible with whole-part dependencies (Wimsatt [1997], [2007]; Craver and Bechtel [2007]). In this context, these 'additional' food-level properties can at least partly be tracked through more sophisticated reductionist models of interacting components.

In the end, one claim motivating nearly all these critiques is that it is because we find these food-level properties that perhaps a sole focus on components will be counter-productive. Since there is no one explicitly arguing that foods are mere aggregates such that no food-level properties exist, everyone's aim is to better understand what foods are, in all their complexity, and for this reductionism is less in opposition to holistic understanding than another way to achieve it. Given this, the question of ontological reductionism, while interesting for raising various philosophical questions, does not seem central.

3.2. Methodological reductionism

A more contentious claim is that a given system is best studied at the lowest possible level, which, in the nutritional context, would entail that food–health interactions are most fruitfully investigated at the level of nutrients or other food components. Many of the above critiques seem to target this assertion, suggesting that methodological reductionism as a research programme focusing on (isolated) components is misguided and should be replaced by (Fardet and Rock [2014]), or at least situated within, alternative frameworks (Tapsell et al. [2016]; Scrinis and Monteiro [2022]).

Now, one strong interpretation of this argument is that methodological reductions to components are problematic per se. In other words, all forms of reductions to this level, be they to nutrient groups or isolated nutrients or components, are problematic because they are studied without explicit reference to the foods or diets containing such nutrients. While such stronger positions are implied by some critics, a more charitable interpretation entails a qualified opposition to methodological reductionism such that its appropriate use and meaning come from situating it within frameworks studying higher levels (Fardet and Rock [2018]), such as foods or dietary patterns. For instance, some claim that dietary pattern research 'is unable to identify the nutrients or interaction patterns involved in disease aetiology, so nutrient-based research is needed to isolate the true causative agents. Nutrient-focused research enhances the mechanistic understanding of food and diet effects' (Tapsell et al. [2016]). Similarly, if food-level properties such as food processing or food synergies are to support an alternative framework (Scrinis

[2013], p. 33; Fardet and Rock [2018]; Scrinis and Monteiro [2022]), they still seem to rely on reductionist methods to tease apart the causal effects of how such processing or food combinations modulate human physiology.

Note that similar to there being no serious case for naïve ontological reductionism, there is no real debate over whether to study these higher-level properties, even if single-component studies dominate the research landscape, as mentioned above. Instead, perhaps the most commonly shared project concerns how to integrate research across various levels (Raubenheimer and Simpson [2016]; Tapsell et al. [2016]; Mattes et al. [2022]). Given this, a more productive framing is one that starts from how evidence from multiple levels can be complementary, a point to which we return in sections 4 and 5.

This qualified appeal to methodological reductionism raises a few interesting issues. Perhaps the most troubling is the implicit or explicit claim that methodological reductionism amounts to nothing more than single-nutrient or single-variable reductionism. Some highlight the limitations of 'the overwhelming focus of nutrition research on single nutrients' (Scrinis [2013], p. 241), of studying 'isolated nutrients, isolated mechanisms of action and isolated health events' (Campbell [2021], p. 496), or assert that a reductionist approach that 'focuses on only one nutrient is especially dangerous' (Tapsell et al. [2016], p. 446). While critics often admit that such reductions can have utility, this framing is problematic as it suggests a false dichotomy between research that reduces to levels of food components—for example, to nutrient categories (such as macronutrients) or single nutrients—versus reductions from higher to lower levels of food assemblages—for example, dietary patterns to diets, to food categories, to specific foods, or to food properties (for example, level of processing). In fact, reductionist programmes need not be committed to reducing to the lowest level, but rather to the most appropriate level for a given question. For instance, there is an entire realm of explanatory possibilities that come from specific reductions to nutrient interactions, such as clarifying how variations in the ratios of nutrients impact health outcomes (Raubenheimer and Simpson [2016]). Moreover, reductionist models need not solely track 'nutrients', but can include any measurable food component to better capture many of the factors often referred to by critics—for example, micronutrients, types of fibre, antioxidants, phytochemicals, polyphenols, carbohydrate cellularity (a form of food matrix), and so on—as well as their interactive effects on important biological parameters. There is no in principle reason why reductionist models cannot track how variations in the intake of multiple interacting

components impact human physiology. While some critics are quick to support 'top-down' approaches, we should first more carefully consider what our best 'bottom-up' approaches entail.

A second issue concerns being able to determine when or whether a reduction to specific components has gone 'too far' or loses its utility. Even within research that views reductions as useful for specifying the putative causative agents in foods or diets, some reasons should be given to help justify when a further reduction of these causal agents to lower levels is no longer appropriate. Likewise, what happens if researchers find that a single component is overwhelmingly responsible for the healthfulness (or harms) of a food or diet? Would this not entail that a reduction to that level is useful regardless of the overarching research paradigm? The issue, which we discuss in section 4, is that of determining how fine-grained these reductions should be.

In sum, the question of how to appropriately employ methodological reductionism is one key part of these various critiques, which can go too far in suggesting that the only reductionist position is that of single-nutrient or single-variable research. Relatedly, Ströhle and Döring ([2010]) posit that moderate reductionism better captures a core aim in nutrition, rather than anti-reductionism. This entails reducing the details and dynamics of nutrient–organism interactions 'as far as possible to those of their components without ignoring the relationship of the system in question with its superior system' (Ströhle and Döring [2010], p. 1397). This is a kind of methodological reductionism, set within a perspective explicitly acknowledging implications at other 'levels' in the system.[5] Even with reductionism so conceived, we face another unresolved issue: for what purpose(s) are researchers carrying out these methodological reductions? Asked in this way, we are led to consider epistemic aims.

3.3. Explanatory or epistemic reductionism

The third issue pertains to the claim that higher level features are best explained by lower levels; accordingly, food–health effects are best explained by nutrients or other food components. In short, reductionism 'tends to explain a phenomenon by dividing it into

[5] Incidentally, we entirely agree with Hoffmann ([2003]) that a 'systems perspective' can be extremely useful and is perhaps necessary to understand complex nutritional problems. As we will develop in a future work, a systems perspective can be based on nutrient-level reductions in ways that satisfy many of the concerns of these critics.

parts' (Fardet and Rock [2014], p. 431). For many critics, the main problem seems to be that such explanations will always be partial or insufficient because the (known or still unmapped) complexity of foods or diets and their health effects cannot be fully accounted for by reductions to components (Moughan [2020]); while reductionism may elucidate some basic mechanisms, 'our knowledge will remain partial and incomplete despite any amount of data' (Fardet and Rock [2014], p. 440). In this sense, some critics converge on Nagel's ([1998]) epistemological anti-reductionism.

Without venturing too deep into philosophical debates about scientific explanations, it is sufficient to raise the question of whether explanations emerging from methodological reductions are only useful when exhaustive. It seems unjustified to attribute to all reductions the epistemic aim of 'nothing-but-ism' (Wimsatt [2006]) or a form of 'greedy reductionism' (Dennett [1996]; Raubenheimer and Simpson [2016]) such that reductions to nutrients or components are carried out in a way that explicitly ignores or skips over other layers and nuances in order to find the foundational layer or factor that explains everything about a food's or diet's healthfulness. Moreover, the critiques based on the claim that we lack 'complete knowledge' about how all aspects of foods have multiple effects on the entire organism suggest an implausibly high standard of explanation. This might be a call for humility, given that nutrition science is relatively young and there is still much that we do not know. However, a more productive question concerns how to evaluate reductions to nutrients in terms of how much they can explain, even if understanding is incomplete.

That said, it is entirely possible that single components can provide explanations of what it is in a food that is primarily responsible for specific outcomes. We explore this in more detail in the section 4, but the main idea is that we need to account for distinct cases: where reductions to a single component provide useful explanations across distinct nutritional frameworks and where reductions may be more judiciously deployed to study causal agents within specific nutritional frameworks (the latter being the targeted use of reductionism promoted by some critics). In both cases, the key explanatory aim seems closer to that of determining when a nutritional factor (or factors) serves as a causal 'difference maker' (Waters [2007]), even if much about the nutritional context remains unknown (more on difference makers below). Those promoting the irreducibility of food-level factors would thereby need to demonstrate that lower-level components simply cannot, or only exceptionally, identify robust causal interactions.

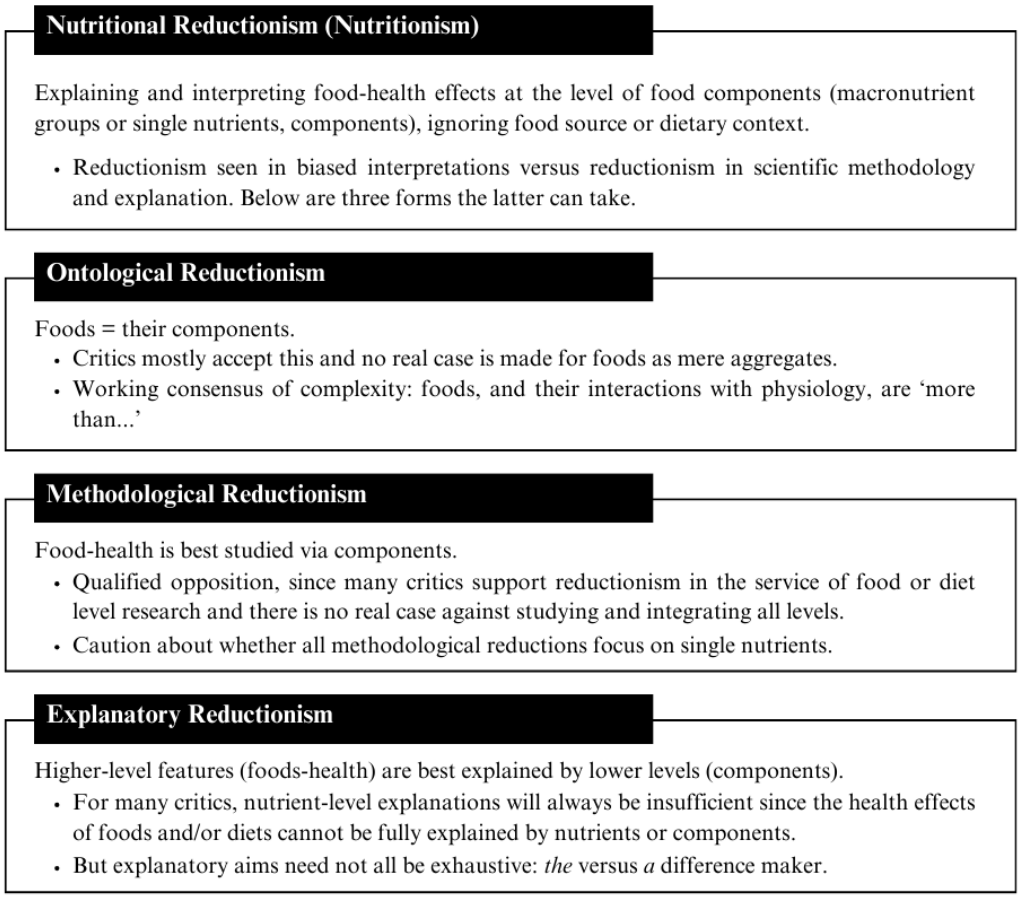

Figure 1. Nutritional reductionism is the broadest term capturing the issues of reductive interpretation and explanation. As our focus is on explanation, we distinguish three forms that 'reductive explanations' can take. For each, the reductionist position is stated, followed by a summary of the issues debated.

Taking stock thus far (summarized in figure 1), one point of contention with these diverse critiques appears to concern the possible uses of methodological reductionism and the explanatory aims of such reductions. There are good reasons to think that methodological reductionism need not be a hindrance to be transcended (Hoffmann [2003]), but quite often enables scientific explanations (Wimsatt [2006]; Ströhle and Döring [2010]; Rosenberg [2020]). While many critics might grant this, it remains unclear why some methodological reductions are ineffective and why others provide useful explanations.

4. Rebuilding the Case for Reductionism

In philosophical literature on causal explanations, one fruitful avenue involves evaluating how causal explanations target an appropriate level for answering a scientific question. According to the manipulationist account (Woodward [2004], [2010]), scientists establish causal relations by specifying what would happen if variables were manipulated: a cause occurs when intervening on one variable reliably produces changes in another. Part of the ensuing causal explanation involves determining when reductions to a specific level give a proportional explanation that neither neglects too much relevant detail nor introduces irrelevant detail: balancing coarse- and fine-grained analyses. This can be illustrated in the example of a chicken sandwich containing copious *Salmonella*, resulting in food poisoning (Bourrat [2018]). While one can correctly appeal to the food level (the sandwich) to explain this outcome, doing so would introduce irrelevant causal details (for example, type of bread), whereas a more precise explanation would focus on the *Salmonella*. Advancing this causal account, Waters ([2007]) adds that scientists do not aim to merely identify any and all causes but those causes that make an actual difference within the context of interest, perhaps the difference, in that variations in one variable partially or fully account for variations in another. The *Salmonella* is arguably the difference maker in the above example (the cause of food poisoning). Not only can nutrition contribute to this literature through its shared project of identifying difference makers, but specifying how this has occurred will better illustrate productive forms of reductionism.

It is generally uncontroversial to single out successes from the so-called golden age of reductionist nutrition research in the early-twentieth century, which involved the isolation and synthesis of all the major nutrients and vitamins, numerous clinical successes with nutrient deficiency diseases, and attempts to establish the recommended daily allowances for calorie and nutrient intake (Carpenter [2003b], [2003c]; Nestle and Nesheim [2012]; Mozaffarian et al. [2018]). During this time, specific micronutrient deficiencies (for example, vitamin C and scurvy), or extreme macronutrient deficiencies (for example, protein and kwashiorkor disease), were identified and nutritional interventions were developed based on a one-nutrient-for-one-disease paradigm (Raubenheimer and Simpson [2016]; Mozaffarian et al. [2018]). This research and the interventions based on it continue in attempts to genetically engineer rice to treat vitamin A deficiency (Tang et

al. [2009]; Wu, Wesseler, et al. [2021]), and could be one way of interpreting the unfortunate introduction of trans fats into foods (Wanders et al. [2017]) or the apparent linear relation between sodium intake and hypertension (Filippini et al. [2022]). In each of these cases, the presence or absence of one food component appears excessively harmful and thus serves as the best candidate for explaining the health effects of foods containing or missing it. Not only has appealing to these specific components provided proportional explanations (which a coarser-grained focus on foods might overcomplicate), but this single-component paradigm helped to establish the nutritional difference makers in these cases. This helps illustrate a stronger epistemic aim of some methodological reductions: to identify the most causally salient factors, which here happen to be nearly exhaustive (the difference makers).

Now, many explanations in nutrition cannot achieve this level of precision, partly because most nutrition-related diseases are complex and multifactorial, thereby requiring a different explanatory framework than was used in the early days of nutrition science (Mozaffarian and Forouhi [2018]; Mozaffarian et al. [2018]). However, instead of suggesting that reductionism is entirely inadequate for this task, amounting to nothing but 'nothing-but-ism', we should consider that in this context (as in other areas of biology; see Lynch et al. [2019]) the explanatory aim can be weakened to finding an actual difference maker (Waters [2007]): the most salient or robust cause among other known or potential causes that partially but significantly explains variations in the outcome of interest. We illustrate this here with a detailed discussion of the so-called diet–heart hypothesis, a central issue facing nutrition science, which Scrinis and others disparagingly view as misguided nutritionism (Jacobs et al. [2009]; Scrinis [2013], chap. 4).

Epidemiological research from the 1960s and 70s sought to explain the worrying rises in cardiovascular diseases (CVD) in various Western countries by studying lifestyle factors. One promising explanation focused on the intriguing correlations between dietary patterns and CVD. The main hypothesis for the relevant difference maker was dietary fat and cholesterol, though the precise causal pathways remained uncertain (Keys et al. [1957]; Anderson et al. [1987]; De Caterina et al. [2006]). Many critics of this 'diet–heart hypothesis' claim that as research was poured into it, this had a negative impact on the development of dietary guidelines based around decreasing fat intake and consuming 'fat-free' foods, which inadvertently led to an increase in consumption of refined carbohydrates, all of which purportedly played some role in the ensuing rise in obesity and

metabolic diseases (Taubes [2001]; Weinberg [2004]). Scrinis ([2013]) judges this hypothesis as committing nutritionism since it exclusively focused on nutrient-level explanations—'dietary fats' and CVD—(generally) isolated from other dietary aspects, distorted public discourse through a vilification of high-fat foods, and led to 'fat-phobic' nutritional policies. As later research appeared to vindicate overall fat consumption (DuBroff and Lorgeril [2021]), this resulted in the seeming reversal from low-fat to pro-fat policies and dietary fads, supposedly providing more reason to condemn reductionist methods.

Before blaming reductionism as such for these apparent contradictions and policies, consider that more epidemiological studies over the intervening years, coupled with technical advances, led to nuanced explanations of the difference makers involved in diet–CVD interactions. This involved a further reduction of 'dietary fats' into saturated, trans, poly- and mono-unsaturated fats, on the one hand, and the biochemical reduction of 'serum cholesterol' into HDL, LDL, VLDL, IDL, apolipoproteins, and so on, and their differential capacity to enter arterial walls. These further reductions allowed for more precise predictions as to which fats were potential or actual difference makers and why, and experimental and well-designed observational studies both added to the manipulationist details about how outcomes vary when types of fats are substituted. We now have evidence spanning controlled trials, prospective cohort studies and systematic reviews suggesting that while dietary cholesterol may not need to be explicitly monitored in otherwise healthy dietary patterns, consumption of specific fats, for example, saturated and trans, are actual difference makers in that they seem to consistently raise the more atherogenic LDL cholesterol in various populations,[6] whereas poly- and mono-unsaturated fats tend to be beneficial or neutral on cholesterol markers and CVD outcomes (Li et al.

[6] Of course, dietary fat is not the only dietary factor that can raise serum cholesterol levels, but we focus on it because it is repeatedly viewed with scepticism by Scrinis and, despite some continued claims to the contrary (Valk et al. [2022]), the weight of evidence strongly supports a reductionist explanation. (For a similar argument based on vitamin C, see (Ströhle and Döring [2010]).) To add further nuance, it appears that the effects of saturated fat (SF) consumption fall along an S-shaped curve such that between roughly 0–10% of total calories there is little to no harm, but around 8–10% the risks increase rapidly before eventually levelling off (Maki et al. [2021]). This can explain why some studies focusing on changes to SF levels beyond 10–15% may show little or contradictory effects from interventions. Also, whether avoiding SF is beneficial or not depends on substitutions: replacing it with high-glycaemic, refined carbohydrates seems equally harmful; replacing it with polyunsaturated fats has strong evidence for being beneficial (Li et al. [2015]). Neither of these findings vindicate SFs and reductionist methods were crucial for all these nuances.

[2015]; Clifton and Keogh [2017]; Sacks et al. [2017]; Hooper et al. [2020]; Mazidi et al. [2020]; Maki et al. [2021]). With strong support for causal links between raised LDL and CVD coming from multiple angles—RCTs, pharmacological and dietary interventions, mechanistic models, and advances in Mendelian randomization—this nuanced form of the 'diet–heart hypothesis' is increasingly robust, or at the very least there is a strong case for taking it seriously (Ference et al. [2017]; Borén et al. [2020]; Mach et al. [2020]; Gaba et al. [2023]). While specific dietary fats may not be the actual difference maker in some CVD outcomes, the evidence strongly supports their role as an actual difference maker.

Critics might retort that the difference-making insights came more from observing that components like 'saturated fats' impact the body differently due to their respective food sources (for example, saturated fats in chocolate versus red meat versus dairy products). While true to a degree, appeals to food sources cannot fully negate the explanatory role of specific fats as difference makers, which at least partly rests on the finding that substituting saturated fats for poly- or monounsaturated fats across food types still appears beneficial, especially when considering overall dose and other components in foods that may mitigate exposures (Sacks et al. [2017]).[7]

Contrary to how this story is often interpreted by critics, it illustrates the need to improve, rather than abandon, reductionist methods. Returning to the supposed historical 'flip-flopping' on fat consumption, further clarification of how specific nutrients interact to influence health outcomes came from researching how the dietary ratios of macronutrients have changed since the 1970s in many countries. With increased production and consumption of readily digestible fats and carbohydrates, two related problems with macronutrients emerged: one the one hand, some dietary fats were replaced with refined carbohydrates, while on the other, food supplies became increasingly protein-diluted (having lower levels of protein relative to non-protein energy), both of which are causal factors explaining increased overall food intake and increased CVD risks (Simpson and Raubenheimer [2005]; Raubenheimer and Simpson [2019]; Wali et al. [2021]; Grech et

[7] Even if foods like chocolate or dairy products contain potentially beneficial forms of saturated fat (steric acid in chocolate) or other components (milk fat globule membrane) that might mitigate other risks, their consumption in otherwise healthy dietary patterns strongly aligns with recommendations to reduce overall saturated fat intake. Given this, when dose is considered, this food-level challenge is largely a moot point for these otherwise robust epidemiological associations.

al. [2022b]).[8] To be clear, misinterpretations of the dietary guidelines that suggested avoiding all fats (rather than just limiting them), which seemingly gave a green light to consuming refined carbohydrates, were naïvely reductionistic given that they overlooked these nutrient substitutions and nutrient–nutrient interactions. However, as with the above examples, it was by finding an appropriate level of reductionist analysis, for example, the interactions of macronutrient ratios within foods and diets, that another crucial difference maker was identified. While a distorted protein to energy ratio is not the difference maker explaining all overeating and CVD outcomes, it is nevertheless an increasingly robust one.

Ultimately, while critics might agree that methodological reductionism can be used well or poorly, they often go on to claim that it either always or mostly gets used poorly, lending itself too easily to misinterpretations, and is thus best viewed with scepticism (Scrinis and Monteiro [2022]). We argue that this is too hasty and that we should more carefully consider when and how reductionism can be used well. In our view, it was precisely because of these reductions to the nutrient level that causal explanations could be made based on identifying the actual difference makers (as with specific deficiencies) or an actual difference maker (as with diet-CVD). What is at stake in such examples is understanding how scientists are repeatedly testing the hypothesis that a reduction to nutrients and other components, likely in some combination, can achieve such an aim. From there, they assess where these explanations run into limitations and how to improve them. The implication is not the need for a new paradigm but the need for clarity about the role reductionism plays in composing the causal-evidential picture. Without this, we risk throwing out the proverbial baby with the bathwater.

With that in mind, we can strengthen this case for reductionism further by addressing the false dichotomy assumed by critics between single-nutrient research and food-diet levels. Over the past 30 or more years, nutritional ecology and related fields have helped to unravel the complexities of how the (macro)nutrients in foods modulate physiology, behaviour, and various biological outcomes (Raubenheimer et al. [2009], [2022]; Simpson and Raubenheimer [2012]; Raubenheimer and Simpson [2016]). By examining this field, we can better understand another important aim of reductionist methods: identifying causal mechanisms.

---

[8] This factor of how protein dilution modulates food intake is discussed in more detail in the next section.

5. Mechanisms and Synthetic Reductionism in Nutritional Ecology

There has been much recent philosophical research into the role of mechanisms for developing nuanced accounts of causal explanations (Machamer et al. [2000]; Bechtel and Richardson [2010]; Craver and Darden [2013]), which Rosenberg suggests may involve reductionism 'with a human face' ([2020]). Instead of claiming that reductions to lower levels capture law-like regularities that would exhaustively explain higher level properties, mechanistic explanations aim to identify and model the key parts and operations responsible for a phenomenon. While at times fragmentary and context-dependent, the resulting explanations can incorporate nuances as to how mechanisms are organized and situated within, or are responsive to, their environment, leading to integrative perspectives (Bechtel [2009]).

Philosophers in these areas have considered a range of examples to test the utility of this approach.[9] As with reductionism, here too nutrition can provide further nuance to these 'decomposition' strategies (Bechtel [2009]) for producing mechanistic explanations, which are crucial for scientific understanding. For instance, part of nutrition science is about reducing 'foods' and decomposing 'feeding behaviours' to the appropriate levels of complexity needed to identify and understand the mechanisms involved. To clarify what is at stake, we take up some insights from the field of nutritional ecology (Raubenheimer et al. [2009]; Simpson and Raubenheimer [2012]; Raubenheimer and Simpson [2016]), which studies how nutrients are often not only more useful than the level of 'foods' for tracking biological outcomes but are perhaps necessary for identifying the biological mechanisms involved and to thereby test predictions. While this may not alleviate all the critics' concerns, reducing foods to specific organizations of nutrients and decomposing the mechanisms by which intake of these nutrients modulates biology has allowed the synthesis of evidence across levels and contexts—looking down in the right place enabled looking around and up.

5.1. Reducing to nutrients and decomposing feeding: nested mechanisms

The field of nutritional ecology takes an explicitly biological approach to understanding nutrient–organism interactions (Raubenheimer et al. [2009], [2012]). As such, it is

[9] As with any area of philosophy, some suggest caution with mechanistic explanations (Nicholson [2012]).

guided by the central questions of why and how organisms select the foods they do, and how these selections affect biological outcomes (for example, lifespan, reproduction, body composition, and so on). To study this, scientists have developed a multidimensional framework called 'nutritional geometry' to track how the food environment impacts biology through distinct nutritional inputs (Raubenheimer et al. [2022]). This involves tracking the ratios of macronutrients, for example, protein to carbohydrate/fat, in the foods that organisms select and combine into meals, and then observing the differential effects of these ratios on fitness, longevity, and other markers (Raubenheimer and Simpson [1997]; Raubenheimer et al. [2009]; Simpson et al. [2015]). A key prediction is that nutrient-specific appetite systems are calibrated by evolution to motivate animals to eat nutrient mixtures that support evolutionary fitness, an outcome that is robustly observed in experimental and field settings (Raubenheimer and Simpson [1997]; Lee et al. [2008]; Jensen et al. [2012]; Guo et al. [2018]). The resulting ratio constitutes the intake target of a 'balanced' diet for that organism. The implication is not that there is a single balanced nutritional mix, but instead that what is optimal varies depending on the biological trait being studied, the environmental constraints at play, and the changing needs of the organism throughout its life course (Raubenheimer et al. [2022]; Sholl [2022]).

While the framework of nutritional geometry is agnostic concerning what parameters to model, the main questions asked have centred around a methodological reduction of foods to macronutrient ratios for two reasons (Raubenheimer and Simpson [2016]). First, macronutrients are a very direct contact between organismal physiology and the food consumed, from taste receptors and digestive enzymes to absorption in the gut and the many metabolic processes that ensue. Second, there are deep evolutionary roots of nutrient-specific appetites for all three macronutrients (in addition to at least two micronutrients: sodium and calcium). The question, then, is whether this reduction to macronutrients can help tame the complexity of dietary variation such that they play the role of an actual difference maker.

One way to answer this has been to investigate this phenomenon of dietary macronutrient balancing on more fine-grained levels and to identify the evolved 'regulatory mechanisms that ensure ingestion of a balanced diet' (Simpson and Raubenheimer [2012]). This entailed a 'downward decomposition' (Bechtel [2009]) of the mechanistic requirements responsible for coordinating the seemingly insurmountable task of consuming the right quantities of nutrients at the right time based on available foods. The result is the

evolution of nested, interconnected mechanisms that span the molecular to behavioural levels (Raubenheimer et al. [2022]; Sholl [2022]): the detection of specific nutrients in the food environment through taste receptors in the mouth, gut, or on appendages, ultimately stimulating or deterring feeding behaviour; the sensing of an internal nutritional state or 'fuel gauge' that tracks circulating and stored nutrients, with the mTOR and AMPK pathways playing key cellular roles in responding to increased or decreased nutrient levels, and a suite of hormones and endocrine signals for responding to specific macronutrients (with fibroblast growth factor 21 (FGF21) as a promising mechanism of protein intake and signal for macronutrient balance (Solon-Biet et al. [2016])); these together produce feedback loops, which entail the mechanism of regulating feeding and general metabolism within a target range relative to changing needs (physio-behavioural 'homeostatic tracking'). These nutrient-specific feedbacks alter the stimuli received from foods, 'resulting in the animal tasting what it needs and eating what it tastes' (Simpson and Raubenheimer [2012], p. 43). With such nested mechanisms that work together and modulate one another, it is already clear that no one part determines the overall operation of nutrient balancing, which will be dependent on the environmental context.

From there, one scientific challenge is to determine whether these mechanisms are anything more than experimental artefacts (Galef [1996]). This can be largely addressed by complementing this downward decomposition by 'looking up' to track these nutrient balancing mechanisms across various contexts. The first layer of context involves comparative research. This capacity to balance intake was studied in numerous, diverse organisms, both experimentally in the lab and in the wild, leading to the finding that when artificially or naturally restricted to foods that are imbalanced with respect to their macronutrient intake target, many (perhaps all) organisms show a strong ability to homeostatically redirect their subsequent eating behaviours to re-approach this target (Raubenheimer and Jones [2006]; Simpson and Raubenheimer [2012]). The result is various sophisticated models showing how and why organisms select the foods they do to approach dietary balance relative to environmental constraints on food availability.

This comparative research provided a strong evolutionary basis from which to ask whether nutrients are also explanatory for human food choices and health outcomes. Here, nutritional ecologists have experimental (randomized control trials) and observational studies in distinct populations showing that humans, like other organisms, indeed homeostatically select foods and compose diets based on nutrient content (Gosby et al.

[2011]; Martinez-Cordero et al. [2012]; Gosby et al. [2014]; Martínez Steele et al. [2018]; Grech et al. [2022b]). Again, even amidst large variations in food sources and meals, nutrient ratios provided a consistently strong explanation of food choices and health outcomes, offering further evidence that these ratios are important nutritional difference makers.

Finally, alongside confirming that nutrient-specific appetites shape food choices in multiple species, we also see how changes in our nutritional environment produce suboptimal outcomes. For instance, given that humans appear to strongly regulate protein intake, when the nutritional environment becomes largely composed of protein-diluted, energy-dense foods, this creates a conflict in our nutrient appetites such that we tend to overeat on these foods to obtain sufficient protein. This is called 'protein leverage' and there are multiple lines of evidence coming from comparative research, and controlled and observational studies in humans, supporting this as an important causal contributor to obesity (Simpson and Raubenheimer [2005]; Gosby et al. [2014]; Hall [2019]; Raubenheimer and Simpson [2019]; Grech et al. [2022b]; Raubenheimer and Simpson [2023]). The hypothesis regarding the role protein leverage plays in obesity is based on our current understanding of the nested mechanisms mentioned, their role in shaping food selection (for example, regulating protein–energy ratios), as well as how this behaviour can come at the expense of health. Modern food environments manipulate or disrupt these evolved appetite systems, producing mismatches on various timescales (Raubenheimer et al. [2012]; Grech et al. [2022b]; Bourrat and Griffiths [forthcoming]).

While macronutrient ratios play a central role in this mechanistic and evidential picture, it is important to note that the reason for focusing on any level within the nutritional hierarchy depends on the question being asked. First, the observation that despite the wide variety of foods consumed in nearly any species, macronutrient ratios remain quite stable and provide robust explanations of patterns in food choices (Chambers et al. [1995]; Raubenheimer and Jones [2006]; Johnson et al. [2013])—being an actual difference maker—would not have been possible if focusing on single nutrients in isolation. Second, we can observe that a further reduction to the elements comprising these nutrients (for example, nitrogen and carbon), while useful in other contexts (Sterner and Elser [2003]), also failed to explain organismal regulation of food selection. These examples illustrate how reductions can go too far for answering specific questions; there are evolved appetites and mechanisms regulating macronutrients (and their ratios) but not

their constituent elements (Raubenheimer et al. [2009]). On the other hand, the food level can be useful for answering questions about the impacts of food selection on the food environment and how this altered ecology feeds back into subsequent food choices and health outcomes (Martínez Steele et al. [2018]). As such, the nutrient and food levels are not in contradiction and nor should they be seen as 'alternative' paradigms; rather they answer different questions and as complementary approaches that, when taken together, provide a richer explanation of food choices and health outcomes.

5.2. Synthetic reductionism

Taken together, we can better clarify the unique form of nutrient-level reductionism at work in nutritional ecology, which might address many of the issues raised by critics. First, we suggest that this field can provide further insights into what Wimsatt ([2006]) calls 'articulatory reductions', where some forms of reduction enable new properties and relations to be discovered, as well as into Bechtel and Richardson's ([2010]) descriptions of mechanistic decomposition. What is at stake is a reduction of 'foods' to nutrients and a decomposition of 'feeding' with the explicit aim to determine which properties of foods, meals, and so on affect our health, the mechanisms by which these interactions occur, and how these mechanisms interact as higher-level units (for example, macronutrient ratios) to comprise difference makers. In this vein, models in nutritional ecology exhibit what we call synthetic reductionism, which are reductions that enable synthetic or integrative explanations. This involves a strategic use of methodological reductionism in that reductions to the nutrient level are necessary to answer specific questions (hence methodological), and these reductions enable new explanations across levels (visualized in figure 2 and explained below).

The left shows a series of methodological reductions or decompositions to increasingly fine-grained levels within the nutritional hierarchy (Raubenheimer and Simpson [2016]). Upon reducing to macronutrients, researchers could identify the explanatory role of the organization of these nutrients into ratios (MNRs) as what differentially impacts behaviour and health. By reducing to this level, it was possible to clarify the mechanisms driving food selection through the evolved appetites for specific nutrients. This mechanistic decomposition helped to show why single-nutrient and even element-based research are counter-productive in that studying these components in isolation is too fine-

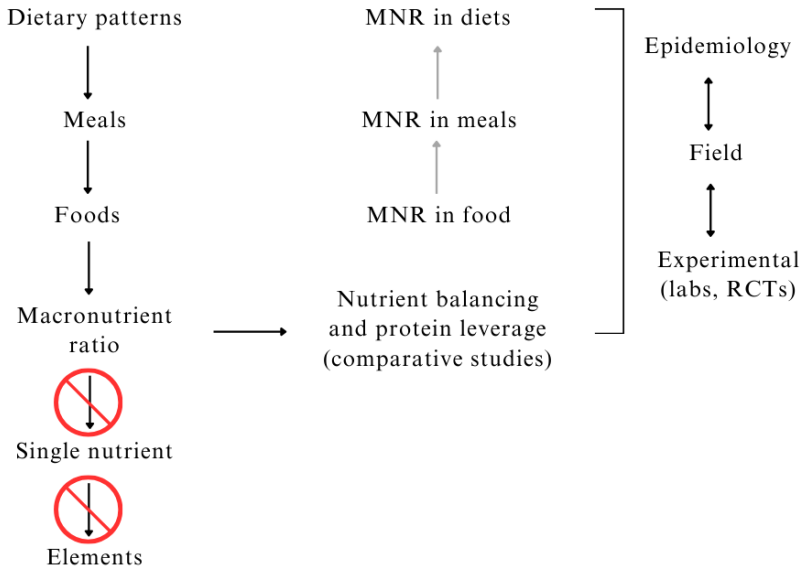

Figure 2. From decomposition to synthesis in nutritional ecology.

grained, missing relevant causal details and thereby failing to identify a reliable difference maker—both of which are clear instances of ineffective or 'greedy reductionism' (Raubenheimer and Simpson [2016]). Accordingly, these mechanisms for nutrient balancing could have remained invisible or largely misunderstood if the reductions stopped at the level of diets or foods or skipped to elements. By going far enough, but not too far, they found a question-appropriate level of reductionism.

Next, arrows marking 'MNR in foods' and so on point to how macronutrient ratios enabled explanatory syntheses: the mechanisms involved in the regulation of MNRs can be observed at the level of foods, meals, or dietary patterns. As such, MNRs perform the role of actual difference makers whose explanatory utility becomes increasingly robust by using distinct methods and study types to test predictions of this model in various contexts, for example, causal validation in controlled experimental studies and ecological relevance from field work and observational studies (Grech et al. [2022a]; Liyanapathirana et al. [2022]). It was by understanding how MNRs modulate outcomes, for example, via the mechanisms of balancing or protein leverage, that explanations could integrate nutrients, food, and diet–health interactions.

One interesting implication is that rather than being intractably complex as anti-reductionists suggest, foods could be called 'robust objects' (Wimsatt [2006]) in that some of their properties (for example, nutrient ratios) provide the bulk of the explanatory

power for their effects on food selection and specific outcomes[10]; as key difference makers, nutrient ratios thereby stipulate some constraints on food-level explanations. Given this, foods are perhaps less complex than they might seem (Raubenheimer and Simpson [2022]), at least with respect to properties that matter for health. Now, while MNRs are one starting point to better understand food–health interactions, this does not mean that MN reductions provide exhaustive or 'nothing-but' explanations, and it is clearly the case that additional aspects are useful to further explain food selection and biological impacts. For instance, we do not always observe that increased protein leads to reduced food intake, that is, protein leverage (Blatt et al. [2011]; Martens et al. [2014]; Fazzino et al. [2023]), and overeating may still occur when protein intake is very low, which some interpret as contradicting this hypothesis (Wu, Li, et al. [2021]; but see Raubenheimer and Simpson [2023]). Consequently, the agenda for synthetic reductionism is to examine which factor(s) interact with MNRs to explain when low protein to non-protein energy does and does not drive excess energy intake. For example, healthy whole-food, largely plant based low protein diets, such as the traditional Okinawan diets are not associated with excess energy intake, likely because of the satiating effect of high fibre content (Raubenheimer and Simpson [2019]).

While much more can be said about this, it at least leaves room for critics to appeal to other nutritional factors. However, as the evidence that MNRs are actual difference makers is sufficiently robust to be taken seriously, the challenge for critics is that of identifying actual difference makers that explain more or explain these causal interactions better than MNRs and nutrient balancing. This will not be a trivial challenge. Although it is early days for translating these nested mechanisms into measurable public health benefits, evidence that diets high in protein relative to other macronutrients are causally associated with decreased energy intake (that is, protein leverage) and fat storage include randomized control trials in free-living (Larsen et al. [2010]; Aller et al. [2014]; Zhu et al. [2021]) and residential settings (Gosby et al. [2011]; Martens et al. [2013]; Campbell et al. [2016]), secondary analyses of combined literature data (Gosby et al. [2014]; Raubenheimer et al. [2015a]) and observational studies of distinct populations (Martinez-Cordero et al. [2012]; Martínez Steele et al. [2018]; Saner et al. [2020], [2023]; Grech et al. [2022b]). Taken together with a growing body of mechanistic evidence for protein

[10] A similar phenomenon can be found in the notion of 'nutritional redundancy' (Wang et al. [2023]).

leverage, this convergence of evidence from human studies involving diverse populations and research contexts is compelling (Raubenheimer and Simpson [2023]). These multiple lines of evidence strongly suggest that subsequent public health interventions will need to work with, rather than against, these nutrient appetites.

Overall, what we call synthetic reductionism seems to imply the exact opposite conclusion of most critics. Better understanding of how nutrient ratios impact health did not require an entirely new paradigm focusing on foods or diets. Instead, it was by pushing reductionism further and identifying difference-making interactions (for example, MNR) among reduced components that the causal connections could be better understood. In other words, the identification of nutrient-level difference makers produced explanations that allowed for the integration of higher levels, both in terms of the organization of nutrients into ratios that we find in foods, meals, diets, and so on, and in terms of the links between biological mechanisms and ecological factors such as food types and availability (for example, protein leverage). While we grant that naïve uses of reductionism can hinder scientific understanding and public health, as can naïve holism, pushing this debate forward requires that we distinguish naïve and constructive uses of reductionism.

6. Conclusions

In this article, we provided the first systematic analysis of the diverse anti-reductionist critiques, showed the extent to which we find them useful, before arguing that some nutrient-level reductions are not only important but indispensable for clarifying key questions within nutrition research. We feel that it is indeed very useful to highlight misinterpretations of scientific evidence, to call out narrowly focused research, and to guard against making hasty generalizations about public health without considering other causal factors within the current totality of evidence. However, against those critiques targeting reductionism per se, a better way forward entails understanding how and when reductions perform useful explanatory roles.

We suggested that this could be accomplished first by reconsidering the stronger and weaker epistemic aims of methodological reductions based on either identifying the or just an actual difference maker. While the earlier successes in the history of nutrition point to ways that the stronger goals of reductionism can be met, it is a persistent challenge in nutrition science to determine the relevant causal difference makers among known and unknown causes. We examined one case in which there is growing scientific

evidence in support of one such difference maker, that is, types of dietary fats and CVD outcomes, which has arguably benefited greatly from reductionist methods.

To provide further support for nutrient-level reductionism, we turned next to the field of nutritional ecology and its dual strategies of reducing foods to macronutrient ratios or mixtures and decomposing feeding behaviours into a nested set of biological mechanisms. The kind of explanations developed in this field help to appreciate how nutrients are a shared explanans across levels in the nutritional hierarchy (foods, meals, diets…). In other words, while the individual foods eaten and the dietary patterns can vary significantly over time, there is strong evidence that this diversity can be clarified through evolved preferences for macronutrient intake patterns. Focusing on this level led to proportional explanations based around macronutrient ratios as key nutritional difference makers.

Moreover, this focus on nutrients can help avoid the problems of being both too reductionist and not enough—either reducing to single nutrients or elements versus focusing on food-level properties as fundamentally irreducible. The issue, as in many cases discussed above, is about how reductionism is utilized and the ability to provide a proportional or difference-making explanation based on that reduction. While each level in the nutritional hierarchy is important for answering different questions, critics of reductionism may find much of interest in the form of methodological reductionism that we call synthetic reductionism, which could uncover common ground between reductionists and holists.

Ultimately, judging reductionism to be a failed methodology in turn fails to appreciate when and how it can be useful. Such claims may even be harmful by presenting a misleadingly fragmented picture of nutritional knowledge (Katz and Meller [2014]), which could inadvertently further tarnish public trust in dietary recommendations. Going forward, it will be useful to reconsider the explanatory potential of reductionist programmes based on careful engagement with science so as not to implicitly distort and inadvertently undermine the integrity of nutrition evidence.

Acknowledgements

Both authors would like to thank the two anonymous referees for their useful suggestions. Jonathan Sholl would especially like to thank his colleagues at ImmunoConcept (University of Bordeaux), particularly Maël Lemoine and Fridolin Gross, and everyone in the

Theory and Method in Biosciences team (University of Sydney) for their kind support and feedback on earlier drafts. More specifically, both authors deeply thank Paul Griffiths for his generosity in making this collaboration possible through his Laureate Fellowship, A Philosophy of Medicine for the 21st Century (FL170100160). David Raubenheimer was supported by the Australian National Health and Medical Research Council (programme grant no. 1149976).

Jonathan Sholl
ImmunoConcept, CNRS UMR 516
Collège Sciences de la Santé
Université de Bordeaux
Bordeaux, France
jonathan.sholl@u-bordeaux.fr

David Raubenheimer
Charles Perkins Centre
School of Life and Environmental Science
The University of Sydney
Sydney, New South Wales, Australia
david.raubenheimer@sydney.edu.au

References

Aguilera, J. M. [2019]: 'The Food Matrix: Implications in Processing, Nutrition, and Health', *Critical Reviews in Food Science and Nutrition*, **59**, pp. 3612–29.

Aller, E. E. J. G., Larsen, T. M., Claus, H., Lindroos, A. K., Kafatos, A., Pfeiffer, A., Martinez, J. A., Handjieva-Darlenska, T., Kunesova, M., Stender, S., Saris, W. H. M., Astrup, A. and van Baak, M. A. [2014]: 'Weight Loss Maintenance in Overweight Subjects on *ad libitum* Diets with High or Low Protein Content and Glycemic Index: The DIOGENES Trial 12-Month Results', *International Journal of Obesity*, **38**, pp. 1511–17.

Anderson, K. M., Castelli, W. P. and Levy, D. [1987]: 'Cholesterol and Mortality: 30 Years of Follow-up from the Framingham Study', *Journal of the American Medical Association*, **257**, pp. 2176–80.

Bechtel, W. [2009]: 'Looking down, around, and Up: Mechanistic Explanation in Psychology', *Philosophical Psychology*, **22**, pp. 543–64.

Bechtel, W. and Richardson, R. C. [2010]: *Discovering Complexity: Decomposition and Localization as Strategies in Scientific Research*, Cambridge, MA: The MIT Press.

Bero, L. A., Norris, S. L. and Lawrence, M. A. [2019]: 'Making Nutrition Guidelines Fit for Purpose', *British Medical Journal*, **365**, available at <doi.org/10.1136/bmj.l1579>.

Blatt, A. D., Roe, L. S. and Rolls, B. J. [2011]: 'Increasing the Protein Content of Meals and Its Effect on Daily Energy Intake', *Journal of the American Dietetic Association*, **111**, pp. 290–94.

Bloor, D. [1991]: *Knowledge and Social Imagery*, Chicago, IL: University of Chicago Press.

Borén, J., Chapman, M. J., Krauss, R. M., Packard, C. J., Bentzon, J. F., Binder, C. J., Daemen, M. J., Demer, L. L., Hegele, R. A., Nicholls, S. J., Nordestgaard, B. G., Watts, G. F., Bruckert, E., Fazio, S., Ference, B. A., Graham, I., Horton, J. D., Landmesser, U., Laufs, U., Masana, L., Pasterkamp, G., Raal, F. J., Ray, K. K., Schunkert, H., Taskinen, M.-R., van de Sluis, B., Wiklund, O., Tokgozoglu, L., Catapano, A. L. and Ginsberg, H. N. [2020]: 'Low-Density Lipoproteins Cause Atherosclerotic Cardiovascular Disease: Pathophysiological, Genetic, and Therapeutic Insights: A Consensus Statement from the European Atherosclerosis Society Consensus Panel', *European Heart Journal*, **41**, pp. 2313–30.

Borghini, A., Piras, N. and Serini, B. [2021]: 'Defective Food Concepts', *Synthese*, **199**, pp. 12225–49.

Bourrat, P. [2018]: 'Have Causal Claims about the Gut Microbiome Been Over-hyped?', *BioEssays*, **40**, available at <doi.org/10.1002/bies.201800178>.

Bourrat, P. and Griffiths, P. E. [forthcoming]: 'The Idea of Mismatch in Evolutionary Medicine', *British Journal for the Philosophy of Science*, **75**, available at <doi.org/10.1086/716543>.

Campbell, C. P., Raubenheimer, D., Badaloo, A. V., Gluckman, P. D., Martinez, C., Gosby, A., Simpson, S. J., Osmond, C., Boyne, M. S. and Forrester, T. E. [2016]: 'Developmental Contributions to Macronutrient Selection: A Randomized Controlled Trial in Adult Survivors of Malnutrition', *Evolution, Medicine, and Public Health*, **2016**, pp. 158–69.

Campbell, T. C. [2021]: 'Nutrition and Medicine: Are They Connected?', *American Journal of Lifestyle Medicine*, **15**, pp. 495–97.

Carpenter, K. J. [2003a]: 'A Short History of Nutritional Science, Part 1 (1785–1885)', *The Journal of Nutrition*, **133**, pp. 638–45.

Carpenter, K. J. [2003b]: 'A Short History of Nutritional Science, Part 2 (1885–1912)', *The Journal of Nutrition*, **133**, pp. 975–84.

Carpenter, K. J. [2003c]: 'A Short History of Nutritional Science, Part 3 (1912–1944)', *The Journal of Nutrition*, **133**, pp. 3023–32.

Carpenter, K. J. [2003d]: 'A Short History of Nutritional Science, Part 4 (1945–1985)', *The Journal of Nutrition*, **133**, pp. 3331–42.

Cena, H. and Calder, P. C. [2020]: 'Defining a Healthy Diet: Evidence for the Role of Contemporary Dietary Patterns in Health and Disease', *Nutrients*, **12**, available at <doi.org/10.3390/nu12020334>.

Chambers, P. G., Simpson, S. J. and Raubenheimer, D. [1995]: 'Behavioural Mechanisms of Nutrient Balancing in *Locusta migratori*a Nymphs', *Animal Behaviour*, **50**, pp. 1513–23.

Clifton, P. M. and Keogh, J. B. [2017]: 'A Systematic Review of the Effect of Dietary Saturated and Polyunsaturated Fat on Heart Disease', *Nutrition, Metabolism, and Cardiovascular Diseases*, **27**, pp. 1060–80.

Craver, C. F. and Bechtel, W. [2007]: 'Top-down Causation without Top-down Causes', *Biology and Philosophy*, **22**, pp. 547–63.

Craver, C. F. and Darden, L. [2013]: *In Search of Mechanisms: Discoveries across the Life Sciences*, Chicago: University of Chicago Press.

De Caterina, R., Zampolli, A., Del Turco, S., Madonna, R. and Massaro, M. [2006]: 'Nutritional Mechanisms That Influence Cardiovascular Disease', *The American Journal of Clinical Nutrition*, **83**, pp. 421–26.

Dennett, D. C. [1996]: *Darwin's Dangerous Idea: Evolution and the Meanings of Life*, New York: Simon and Schuster.

Diekman, C., Ryan, C. D. and Oliver, T. L. [2023]: 'Misinformation and Disinformation in Food Science and Nutrition: Impact on Practice', *The Journal of Nutrition*, **153**, pp. 3–9.

DuBroff, R. and Lorgeril, M. de [2021]: 'Fat or Fiction: The Diet–Heart Hypothesis', *BMJ Evidence-Based Medicine*, **26**, pp. 3–7.

Fabbri, A., Chartres, N., Scrinis, G. and Bero, L. A. [2017]: 'Study Sponsorship and the Nutrition Research Agenda: Analysis of Randomized Controlled Trials Included in Systematic Reviews of Nutrition Interventions to Address Obesity', *Public Health Nutrition*, **20**, pp. 1306–13.

Fardet, A. and Rock, E. [2014]: 'Toward a New Philosophy of Preventive Nutrition: From a Reductionist to a Holistic Paradigm to Improve Nutritional Recommendations', *Advances in Nutrition*, **5**, pp. 430–46.

Fardet, A. and Rock, E. [2018]: 'Perspective: Reductionist Nutrition Research Has Meaning Only within the Framework of Holistic and Ethical Thinking', *Advances in Nutrition*, **9**, pp. 655–70.

Fardet, A. and Rock, E. [2020]: 'Exclusive Reductionism, Chronic Diseases, and Nutritional Confusion: The Degree of Processing as a Lever for Improving Public Health', *Critical Reviews in Food Science and Nutrition*, **62**, pp. 2784–99.

Fazzino, T. L., Courville, A. B., Guo, J. and Hall, K. [2023]: '*Ad libitum* Meal Energy Intake Is Positively Influenced by Energy Density, Eating Rate, and Hyper-palatable Food across Four Dietary Patterns', *Nature Food*, **4**, pp. 144–47.

Ference, B. A., Ginsberg, H. N., Graham, I., Ray, K. K., Packard, C. J., Bruckert, E., Hegele, R. A., Krauss, R. M., Raal, F. J., Schunkert, H., Watts, G. F., Borén, J., Fazio, S., Horton, J. D., Masana, L., Nicholls, S. J., Nordestgaard, B. G., van de Sluis, B., Taskinen, M.-R., Tokgözoğlu, L., Landmesser, U., Laufs, U., Wiklund, O., Stock, J. K., Chapman, M. J. and Catapano, A. L. [2017]: 'Low-Density Lipoproteins Cause Atherosclerotic Cardiovascular Disease, 1: Evidence from Genetic, Epidemiologic,

and Clinical Studies. A Consensus Statement from the European Atherosclerosis Society Consensus Panel', *European Heart Journal*, **38**, pp. 2459–72.

Filippini, T., Malavolti, M., Whelton, P. K. and Vinceti, M. [2022]: 'Sodium Intake and Risk of Hypertension: A Systematic Review and Dose–Response Meta-analysis of Observational Cohort Studies', *Current Hypertension Reports*, **24**, pp. 133–44.

Folker, A. P. and Sandøe, P. [2008]: 'Leaping "Out of the Doubt"—Nutrition Advice: Values at Stake in Communicating Scientific Uncertainty to the Public', *Health Care Analysis*, **16**, pp. 176–91.

Gaba, P., O'Donoghue, M. L., Park, J.-G., Wiviott, S. D., Atar, D., Kuder, J. F., Im, K., Murphy, S. A., De Ferrari, G. M., Gaciong, Z. A., Toth, K., Gouni-Berthold, I., Lopez-Miranda, J., Schiele, F., Mach, F., Flores-Arredondo, J. H., López, J. A. G., Elliott-Davey, M., Wang, B., Monsalvo, M. L., Abbasi, S., Giugliano, R. P. and Sabatine, M. S. [2023]: 'Association between Achieved Low-Density Lipoprotein Cholesterol Levels and Long-Term Cardiovascular and Safety Outcomes: An Analysis of FOURIER-OLE', *Circulation*, **147**, pp. 1192–203.

Galef, B. G. [1996]: 'Food Selection: Problems in Understanding How We Choose Foods to Eat', *Neuroscience and Biobehavioral Reviews*, **20**, pp. 67–73.

Gatherer, D. [2010]: 'So What Do We Really Mean When We Say That Systems Biology Is Holistic?', *BMC Systems Biology*, **4**, available at <doi.org/10.1186/1752-0509-4-22>.

Gosby, A. K., Conigrave, A. D., Lau, N. S., Iglesias, M. A., Hall, R. M., Jebb, S. A., Brand-Miller, J., Caterson, I. D., Raubenheimer, D. and Simpson, S. J. [2011]: 'Testing Protein Leverage in Lean Humans: A Randomised Controlled Experimental Study', *PLOS One*, **6**, available at <doi.org/10.1371/journal.pone.0025929>.

Gosby, A. K., Conigrave, A. D., Raubenheimer, D. and Simpson, S. J. [2014]: 'Protein Leverage and Energy Intake', *Obesity Reviews*, **15**, pp. 183–91.

Grantham, T. A. [2004]: 'Conceptualizing the (Dis)Unity of Science', *Philosophy of Science*, **71**, pp. 133–55.

Grech, A., Rangan, A., Allman-Farinelli, M., Simpson, S. J., Gill, T. and Raubenheimer, D. [2022a]: 'A Comparison of the Australian Dietary Guidelines to the NOVA Classification System in Classifying Foods to Predict Energy Intakes and Body Mass Index', *Nutrients*, **14**, available at <doi.org/10.3390/nu14193942>.

Grech, A., Sui, Z., Rangan, A., Simpson, S. J., Coogan, S. C. P. and Raubenheimer, D. [2022b]: 'Macronutrient (Im)Balance Drives Energy Intake in an Obesogenic Food Environment: An Ecological Analysis', *Obesity*, **30**, pp. 2156–66.

Guo, S.-T., Hou, R., Garber, P. A., Raubenheimer, D., Righini, N., Ji, W.-H., Jay, O., He, S.-J., Wu, F., Li, F.-F. and Li, B.-G. [2018]: 'Nutrient-Specific Compensation for Seasonal Cold Stress in a Free-Ranging Temperate Colobine Monkey', *Functional Ecology*, **32**, pp. 2170–80.

Guyenet, S. [2023]: 'Read This, Not That: The Hidden Cost of Nutrition Misinformation', *Asterisk Magazine*, <asteriskmag.com/issues/2/read-this-not-that-the-hidden-cost-of-nutrition-misinformation>.

Hall, K. [2019]: 'The Potential Role of Protein Leverage in the US Obesity Epidemic', *Obesity*, **27**, pp. 1222–24.

Hercberg, S. [2005]: 'The History of β-Carotene and Cancers: From Observational to Intervention Studies. What Lessons Can Be Drawn for Future Research on Polyphenols?', *The American Journal of Clinical Nutrition*, **81**, pp. 218–22.

Hoffmann, I. [2003]: 'Transcending Reductionism in Nutrition Research', *The American Journal of Clinical Nutrition*, **78**, pp. 514–16.

Hooper, L., Martin, N., Jimoh, O. F., Kirk, C., Foster, E. and Abdelhamid, A. S. [2020]: 'Reduction in Saturated Fat Intake for Cardiovascular Disease', *The Cochrane Database of Systematic Reviews*, **5**, available at <doi.org/10.1002/14651858.CD011737.pub2>.

Hu, F. B. [2002]: 'Dietary Pattern Analysis: A New Direction in Nutritional Epidemiology', *Current Opinion in Lipidology*, **13**, pp. 3–9.

Jacobs, D. R. and Tapsell, L. C. [2008]: 'Food, Not Nutrients, Is the Fundamental Unit in Nutrition', *Nutrition Reviews*, **65**, pp. 439–50.

Jacobs, D. R., Gross, M. D. and Tapsell, L. C. [2009]: 'Food Synergy: An Operational Concept for Understanding Nutrition', *The American Journal of Clinical Nutrition*, **89**, pp. 1543–48.

Jacobs, D. R. and Tapsell, L. C. [2013]: 'Food Synergy: The Key to a Healthy Diet', *Proceedings of the Nutrition Society*, **72**, pp. 200–6.

Jensen, K., Mayntz, D., Toft, S., Clissold, F. J., Hunt, J., Raubenheimer, D. and Simpson, S. J. [2012]: 'Optimal Foraging for Specific Nutrients in Predatory Beetles', *Proceedings of the Royal Society B*, **279**, pp. 2212–18.

Johnson, C. A., Raubenheimer, D., Rothman, J. M., Clarke, D. and Swedell, L. [2013]: '30 Days in the Life: Daily Nutrient Balancing in a Wild Chacma Baboon', *PLOS One*, **8**, available at <doi.org/10.1371/journal.pone.0070383>.

Jukola, S. [2019]: 'On the Evidentiary Standards for Nutrition Advice', *Studies in History and Philosophy of Biological and Biomedical Sciences*, **73**, pp. 1–9.

Jukola, S. [2021]: 'Commercial Interests, Agenda Setting, and the Epistemic Trustworthiness of Nutrition Science', *Synthese*, **198**, pp. 2629–46.

Katz, D. L. and Meller, S. [2014]: 'Can We Say What Diet Is Best for Health?', *Annual Review of Public Health*, **35**, pp. 83–103.

Keys, A., Anderson, J. and Grande, F. [1957]: 'Prediction of Serum-Cholesterol Responses of Man to Changes in Fats in the Diet', *The Lancet*, **270**, pp. 959–66.

Kroker-Lobos, M. F., Mazariegos, M., Guamuch, M. and Ramirez-Zea, M. [2022]: 'Ultraprocessed Products as Food Fortification Alternatives: A Critical Appraisal from Latin America', *Nutrients*, **14**, available at <doi.org/10.3390/nu14071413>.

Larsen, T. M., Dalskov, S.-M., van Baak, M., Jebb, S. A., Papadaki, A., Pfeiffer, A. F. H., Martinez, J. A., Handjieva-Darlenska, T., Kunešová, M., Pihlsgård, M., Stender, S., Holst, C., Saris, W. H. M. and Astrup, A. [2010]: 'Diets with High or Low Protein Content and Glycemic Index for Weight-Loss Maintenance', *New England Journal of Medicine*, **363**, pp. 2102–13.

Lawrence, M., Naude, C., Armstrong, R., Bero, L., Covic, N., Durao, S., Ghersi, D., Macdonald, G., MacLehose, H., Margetts, B., Tovey, D., Volmink, J. and Young, T. [2016]: 'A Call to Action to Reshape Evidence Synthesis and Use for Nutrition Policy', *Cochrane Database of Systematic Reviews*, **11**, available at <doi.org//10.1002/14651858.ED000118>.

Lee, K. P., Simpson, S. J., Clissold, F. J., Brooks, R., Ballard, J. W. O., Taylor, P. W., Soran, N. and Raubenheimer, D. [2008]: 'Lifespan and Reproduction in *Drosophila*: New Insights from Nutritional Geometry', *Proceedings of the National Academy of Sciences USA*, **105**, pp. 2498–503.

Levy, N. [2018]: 'Taking Responsibility for Health in an Epistemically Polluted Environment', *Theoretical Medicine and Bioethics*, **39**, pp. 123–41.

Li, Y., Hruby, A., Bernstein, A. M., Ley, S. H., Wang, D. D., Chiuve, S. E., Sampson, L., Rexrode, K. M., Rimm, E. B., Willett, W. C. and Hu, F. B. [2015]: 'Saturated Fats Compared with Unsaturated Fats and Sources of Carbohydrates in Relation to Risk of Coronary Heart Disease: A Prospective Cohort Study', *Journal of the American College of Cardiology*, **66**, pp. 1538–48.

Liyanapathirana, N. N., Grech, A., Li, M., Malik, A., Lenzen, M. and Raubenheimer, D. [2022]: 'Nutrient-Sensitive Approach for Sustainability Assessment of Different Dietary Patterns in Australia', *The American Journal of Clinical Nutrition*, **115**, pp. 1048–58.

Ludwig, D. S., Willett, W. C., Volek, J. S. and Neuhouser, M. L. [2018]: 'Dietary Fat: From Foe to Friend?', *Science*, **362**, pp. 764–70.

Lynch, K. E., Parke, E. C. and O'Malley, M. A. [2019]: 'How Causal Are Microbiomes? A Comparison with the *Helicobacter pylori* Explanation of Ulcers', *Biology and Philosophy*, **34**, available at <doi.org/10.1007/s10539-019-9702-2>.

Mach, F., Baigent, C., Catapano, A. L., Koskinas, K. C., Casula, M., Badimon, L., Chapman, M. J., De Backer, G. G., Delgado, V., Ference, B. A., Graham, I. M., Halliday, A., Landmesser, U., Mihaylova, B., Pedersen, T. R., Riccardi, G., Richter, D. J., Sabatine, M. S., Taskinen, M.-R., Tokgozoglu, L., Wiklund, O. and ESC Scientific Document Group [2020]: '2019 ESC/EAS Guidelines for the Management of Dyslipidaemias: Lipid Modification to Reduce Cardiovascular Risk: The Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)', *European Heart Journal*, **41**, pp. 111–88.

Machamer, P., Darden, L. and Craver, C. F. [2000]: 'Thinking about Mechanisms', *Philosophy of Science*, **67**, pp. 1–25.

Maki, K. C., Dicklin, M. R. and Kirkpatrick, C. F. [2021]: 'Saturated Fats and Cardiovascular Health: Current Evidence and Controversies', *Journal of Clinical Lipidology*, **15**, pp. 765–72.

Martens, E. A., Lemmens, S. G. and Westerterp-Plantenga, M. S. [2013]: 'Protein Leverage Affects Energy Intake of High-Protein Diets in Humans', *The American Journal of Clinical Nutrition*, **97**, pp. 86–93.

Martens, E. A., Tan, S.-Y., Dunlop, M. V., Mattes, R. D. and Westerterp-Plantenga, M. S. [2014]: 'Protein Leverage Effects of Beef Protein on Energy Intake in Humans', *The American Journal of Clinical Nutrition*, **99**, pp. 1397–406.

Martínez Steele, E., Raubenheimer, D., Simpson, S. J., Baraldi, L. G. and Monteiro, C. A. [2018]: 'Ultra-processed Foods, Protein Leverage, and Energy Intake in the USA', *Public Health Nutrition*, **21**, pp. 114–24.

Martinez-Cordero, C., Kuzawa, C. W., Sloboda, D. M., Stewart, J., Simpson, S. J. and Raubenheimer, D. [2012]: 'Testing the Protein Leverage Hypothesis in a Free-Living Human Population', *Appetite*, **59**, pp. 312–15.

Mattes, R. D., Rowe, S. B., Ohlhorst, S. D., Brown, A. W., Hoffman, D. J., Liska, D. J., Feskens, E. J. M., Dhillon, J., Tucker, K. L., Epstein, L. H., Neufeld, L. M., Kelley, M., Fukagawa, N. K., Sunde, R. A., Zeisel, S. H., Basile, A. J., Borth, L. E. and Jackson, E. [2022]: 'Valuing the Diversity of Research Methods to Advance Nutrition Science', *Advances in Nutrition*, **13**, pp. 1324–93.

Maximova, K., Khodayari Moez, E., Dabravolskaj, J., Ferdinands, A. R., Dinu, I., Lo Siou, G., Al Rajabi, A. and Veugelers, P. J. [2020]: 'Co-consumption of Vegetables and Fruit, Whole Grains, and Fiber Reduces the Cancer Risk of Red and Processed Meat in a Large Prospective Cohort of Adults from Alberta's Tomorrow Project', *Nutrients*, **12**, available at <doi.org/10.3390/nu12082265>.

Mayne, S. T., Playdon, M. C. and Rock, C. L. [2016]: 'Diet, Nutrition, and Cancer: Past, Present, and Future', *Nature Reviews Clinical Oncology*, **13**, pp. 504–15.

Mazidi, M., Mikhailidis, D. P., Sattar, N., Toth, P. P., Judd, S., Blaha, M. J., Hernandez, A. V., Penson, P. E. and Banach, M. [2020]: 'Association of Types of Dietary Fats and All-Cause and Cause-Specific Mortality: A Prospective Cohort Study and Meta-analysis of Prospective Studies with 1,164,029 Participants', *Clinical Nutrition*, **39**, pp. 3677–86.

Messina, M., Lampe, J. W., Birt, D. F., Appel, L. J., Pivonka, E., Berry, B. and Jacobs, D. R. [2001]: 'Reductionism and the Narrowing Nutrition Perspective', *Journal of the American Dietetic Association*, **101**, pp. 1416–19.

Moughan, P. J. [2020]: 'Holistic Properties of Foods: A Changing Paradigm in Human Nutrition', *Journal of the Science of Food and Agriculture*, **100**, pp. 5056–63.

Mozaffarian, D. and Forouhi, N. G. [2018]: 'Dietary Guidelines and Health: Is Nutrition Science up to the Task?', *British Medical Journal*, **360**, available at <doi.org/10.1136/bmj.k822>.

Mozaffarian, D., Rosenberg, I. and Uauy, R. [2018]: 'History of Modern Nutrition Science: Implications for Current Research, Dietary Guidelines, and Food Policy', *British Medical Journal*, **361**, available at <doi.org/10.1136/bmj.k2392>.

Nagel, T. [1998]: 'Reductionism and Antireductionism', in G. R. Bock and J. A. Goode (*eds*), *The Limits of Reductionism in Biology*, Chichester: John Wiley, pp. 3–14.

Nestle, M. [2007]: *Food Politics: How the Food Industry Influences Nutrition and Health*, Berkeley, CA: University of California Press.

Nestle, M. and Nesheim, M. C. [2012]: 'Why Calories Count: From Science to Politics', Berkeley, CA: University of California Press.

Nicholson, D. [2012]: 'The Concept of Mechanism in Biology', *Studies in History and Philosophy of Biological and Biomedical Sciences*, **43**, pp. 152–63.

Pollan, M. [2007]: 'Unhappy Meals', *New York Times Magazine*, available at <www.nytimes.com/2007/01/28/magazine/28nutritionism.t.html>.

Raubenheimer, D. and Simpson, S. J. [1997]: 'Integrative Models of Nutrient Balancing: Application to Insects and Vertebrates', *Nutrition Research Reviews*, **10**, pp. 151–79.

Raubenheimer, D. and Jones, S. A. [2006]: 'Nutritional Imbalance in an Extreme Generalist Omnivore: Tolerance and Recovery through Complementary Food Selection', *Animal Behaviour*, **71**, pp. 1253–62.

Raubenheimer, D., Simpson, S. J. and Mayntz, D. [2009]: 'Nutrition, Ecology, and Nutritional Ecology: Toward an Integrated Framework', *Functional Ecology*, **23**, pp. 4–16.

Raubenheimer, D., Simpson, S. J. and Tait, A. H. [2012]: 'Match and Mismatch: Conservation Physiology, Nutritional Ecology, and the Timescales of Biological Adaptation', *Philosophical Transactions of the Royal Society B*, **367**, pp. 1628–46.

Raubenheimer, D., Gosby, A. K. and Simpson, S. J. [2015a]: 'Integrating Nutrients, Foods, Diets, and Appetites with Obesity and Cardiometabolic Health', *Obesity*, **23**, pp. 1741–42.

Raubenheimer, D., Machovsky-Capuska, G. E., Gosby, A. K. and Simpson, S. [2015b]: 'Nutritional Ecology of Obesity: From Humans to Companion Animals', *British Journal of Nutrition*, **113**, pp. 26–39.

Raubenheimer, D. and Simpson, S. J. [2016]: 'Nutritional Ecology and Human Health', *Annual Review of Nutrition*, **36**, pp. 603–26.

Raubenheimer, D. and Simpson, S. J. [2019]: 'Protein Leverage: Theoretical Foundations and Ten Points of Clarification', *Obesity*, **27**, pp. 1225–38.

Raubenheimer, D. and Simpson, S. J. [2020]: *Eat Like the Animals: What Nature Teaches Us about the Science of Healthy Eating*, Boston, MA: Houghton Mifflin Harcourt.

Raubenheimer, D., Senior, A. M., Mirth, C., Cui, Z., Hou, R., Le Couteur, D. G., Solon-Biet, S. M., Léopold, P. and Simpson, S. J. [2022]: 'An Integrative Approach to Dietary Balance across the Life Course', *iScience*, **25**, available at <doi.org/10.1016/j.isci.2022.104315>.

Raubenheimer, D. and Simpson, S. J. [2022]: 'Ecology, Protein Leverage, and Public Health', in P. G. Kopelman, I. D. Caterson and W. H. Dietz (*eds*), *Clinical Obesity in Adults and Children*, Malden, MA: John Wiley, pp. 72–88.

Raubenheimer, D. and Simpson, S. J. [2023]: 'Protein Appetite as an Integrator in the Obesity System: The Protein Leverage Hypothesis', *Philosophical Transactions of the Royal Society B*, **378**, available at <doi.org/10.1098/rstb.2022.0212>.

Rees, W. D. [2019]: 'Interactions between Nutrients in the Maternal Diet and the Implications for the Long-Term Health of the Offspring', *Proceedings of the Nutrition Society*, **78**, pp. 88–96.

Rosenberg, A. [2007]: 'Reductionism (and Antireductionism) in Biology', in D. L. Hull and M. Ruse (*eds*), *The Cambridge Companion to the Philosophy of Biology*, Cambridge: Cambridge University Press, pp. 120–38.

Rosenberg, A. [2020]: *Reduction and Mechanism*, Cambridge: Cambridge University Press.

Sacks, F. M., Lichtenstein, A. H., Wu, J. H. Y., Appel, L. J., Creager, M. A., Kris-Etherton, P. M., Miller, M., Rimm, E. B., Rudel, L. L., Robinson, J. G., Stone, N. J. and Van Horn, L. V. [2017]: 'Dietary Fats and Cardiovascular Disease: A Presidential Advisory from the American Heart Association', *Circulation*, **136**, available at <doi.org/10.1161/CIR.0000000000000510>.

Saner, C., Tassoni, D., Harcourt, B. E., Kao, K.-T., Alexander, E. J., McCallum, Z., Olds, T., Rowlands, A. V., Burgner, D. P., Simpson, S. J., Raubenheimer, D., Senior, A. M., Juonala, M. and Sabin, M. A. [2020]: 'Evidence for Protein Leverage in Children and Adolescents with Obesity', *Obesity*, **28**, pp. 822–29.

Saner, C., Senior, A. M., Zhang, H., Eloranta, A.-M., Magnussen, C. G., Sabin, M. A., Juonala, M., Janner, M., Burgner, D. P., Schwab, U., Haapala, E. A., Heitmann, B. L., Simpson, S. J., Raubenheimer, D. and Lakka, T. A. [2023]: 'Evidence for Protein Leverage in a General Population Sample of Children and Adolescents', *European Journal of Clinical Nutrition*, **77**, pp. 652–59.

Scrinis, G. [2008]: 'On the Ideology of Nutritionism', *Gastronomica*, **8**, pp. 39–48.

Scrinis, G. [2012]: 'Nutritionism and Functional Foods', in D. M. Kaplan (*ed.*), *The Philosophy of Food*, Berkeley, CA: University of California Press, pp. 269–91.

Scrinis, G. [2013]: *Nutritionism: The Science and Politics of Dietary Advice*, New York: Columbia University Press.

Scrinis, G. and Monteiro, C. A. [2018]: 'Ultra-processed Foods and the Limits of Product Reformulation', *Public Health Nutrition*, **21**, pp. 247–52.

Scrinis, G. [2020]: 'Ultra-processed Foods and the Corporate Capture of Nutrition', *British Medical Journal*, **371**, available at <doi.org/10.1136/bmj.m4601>.

Scrinis, G. and Monteiro, C. A. [2022]: 'From Ultra-processed Foods to Ultra-processed Dietary Patterns', *Nature Food*, **3**, pp. 671–73.

Shao, A., Drewnowski, A., Willcox, D. C., Krämer, L., Lausted, C., Eggersdorfer, M., Mathers, J., Bell, J. D., Randolph, R. K., Witkamp, R. and Griffiths, J. C. [2017]: 'Optimal Nutrition and the Ever-Changing Dietary Landscape: A Conference Report', *European Journal of Nutrition*, **56**, pp. 1–21.

Sholl, J. [2022]: 'Everything in Moderation or Moderating Everything? Nutrient Balancing in the Context of Evolution and Cancer Metabolism', *Biology and Philosophy*, **37**, available at <doi.org/10.1007/s10539-022-09845-2>.

Siipi, H. [2013]: 'Is Natural Food Healthy?', *Journal of Agricultural and Environmental Ethics*, **26**, pp. 797–812.

Simpson, S. J. and Raubenheimer, D. [2005]: 'Obesity: The Protein Leverage Hypothesis', *Obesity Reviews*, **6**, pp. 133–42.

Simpson, S. J. and Raubenheimer, D. [2012]: *The Nature of Nutrition: A Unifying Framework from Animal Adaptation to Human Obesity*, Princeton, NJ: Princeton University Press.

Simpson, S. J., Le Couteur, D. G. and Raubenheimer, D. [2015]: 'Putting the Balance Back in Diet', *Cell*, **161**, pp. 18–23.

Solon-Biet, S. M., Cogger, V. C., Pulpitel, T., Heblinski, M., Wahl, D., McMahon, A. C., Warren, A., Durrant-Whyte, J., Walters, K. A., Krycer, J. R., Ponton, F., Gokarn, R., Wali, J. A., Ruohonen, K., Conigrave, A. D., James, D. E., Raubenheimer, D., Morrison, C. D., Le Couteur, D. G. and Simpson, S. J. [2016]: 'Defining the Nutritional and Metabolic Context of FGF21 Using the Geometric Framework', *Cell Metabolism*, **24**, pp. 555–65.

Spector, T. D. and Gardner, C. D. [2020]: 'Challenges and Opportunities for Better Nutrition Science', *British Medical Journal*, **369**, available at <doi.org/10.1136/bmj.m2470>.

Sterner, R. W. and Elser, J. J. [2003]: *Ecological Stoichiometry: The Biology of Elements from Molecules to the Biosphere*, Princeton, NJ: Princeton University Press.

Ströhle, A. and Döring, F. [2010]: 'Molecularization in Nutritional Science: A View from Philosophy of Science', *Molecular Nutrition and Food Research*, **54**, pp. 1385–404.

Tang, G., Qin, J., Dolnikowski, G. G., Russell, R. M. and Grusak, M. A. [2009]: 'Golden Rice Is an Effective Source of Vitamin A', *The American Journal of Clinical Nutrition*, **89**, pp. 1776–83.

Tapsell, L. C., Neale, E. P., Satija, A. and Hu, F. B. [2016]: 'Foods, Nutrients, and Dietary Patterns: Interconnections and Implications for Dietary Guidelines', *Advances in Nutrition*, **7**, pp. 445–54.

Taubes, G. [2001]: 'The Soft Science of Dietary Fat', *Science*, **291**, pp. 2536–45.

Temple, N. J. [2023]: 'Research Strategies in Nutrition in Health and Disease: The Failure of Mechanistic Research', *Frontiers in Nutrition*, **10**, <doi.org/10.3389/fnut.2023.1082182>.

Valk, R., Hammill, J. and Grip, J. [2022]: 'Saturated Fat: Villain and Bogeyman in the Development of Cardiovascular Disease?', *European Journal of Preventive Cardiology*, **29**, pp. 2312–21.

Wali, J. A., Raubenheimer, D., Senior, A. M., Le Couteur, D. G. and Simpson, S. J. [2021]: 'Cardio-metabolic Consequences of Dietary Carbohydrates: Reconciling Contradictions Using Nutritional Geometry', *Cardiovascular Research*, **117**, pp. 386–401.

Wanders, A. J., Zock, P. L. and Brouwer, I. A. [2017]: 'Trans Fat Intake and Its Dietary Sources in General Populations Worldwide: A Systematic Review', *Nutrients*, **9**, p. available at <doi.org/10.3390/nu9080840>.

Wang, X.-W., Hu, Y., Menichetti, G., Grodstein, F., Bhupathiraju, S. N., Sun, Q., Zhang, X., Hu, F. B., Weiss, S. T. and Liu, Y.-Y. [2023]: 'Nutritional Redundancy in the Human Diet and Its Application in Phenotype Association Studies', *Nature Communications*, **14**, available at <doi.org/10.1038/s41467-023-39836-0>.

Wang, Y., McKee, M., Torbica, A. and Stuckler, D. [2019]: 'Systematic Literature Review on the Spread of Health-Related Misinformation on Social Media', *Social Science and Medicine*, **240**, available at <doi.org/10.1016/j.socscimed.2019.112552>.

Waters, C. K. [2007]: 'Causes That Make a Difference', *Journal of Philosophy*, **104**, pp. 551–79.

Weinberg, S. L. [2004]: 'The Diet–Heart Hypothesis: A Critique', *Journal of the American College of Cardiology*, **43**, pp. 731–33.

Wimsatt, W. C. [1997]: 'Aggregativity: Reductive Heuristics for Finding Emergence', *Philosophy of Science*, **64**, pp. S372–84.

Wimsatt, W. C. [2006]: 'Reductionism and Its Heuristics: Making Methodological Reductionism Honest', *Synthese*, **151**, pp. 445–75.

Wimsatt, W. C. [2007]: *Re-engineering Philosophy for Limited Beings: Piecewise Approximations to Reality*, Cambridge, MA: Harvard University Press.

Woodward, J. [2004]: *Making Things Happen*, Oxford: Oxford University Press.

Woodward, J. [2010]: 'Causation in Biology: Stability, Specificity, and the Choice of Levels of Explanation', *Biology and Philosophy*, **25**, pp. 287–318.

Wu, F., Wesseler, J., Zilberman, D., Russell, R. M., Chen, C. and Dubock, A. C. [2021]: 'Allow Golden Rice to Save Lives', *Proceedings of the National Academy of Sciences USA*, **118**, available at <doi.org/10.1073/pnas.2120901118>.

Wu, Y., Li, B., Li, L., Mitchell, S. E., Green, C. L., D'Agostino, G., Wang, G., Wang, L., Li, M., Li, J., Niu, C., Jin, Z., Wang, A., Zheng, Y., Douglas, A. and Speakman, J. R. [2021]: 'Very-Low-Protein Diets Lead to Reduced Food Intake and Weight Loss, Linked to Inhibition of Hypothalamic mTOR Signaling, in Mice', *Cell Metabolism*, **33**, pp. 888–904.

Zeisel, S. H., Allen, L. H., Coburn, S. P., Erdman, J. W., Failla, M. L., Freake, H. C., King, J. C. and Storch, J. [2001]: 'Nutrition: A Reservoir for Integrative Science', *The Journal of Nutrition*, **131**, pp. 1319–21.

Zhu, R., Fogelholm, M., Larsen, T. M., Poppitt, S. D., Silvestre, M. P., Vestentoft, P. S., Jalo, E., Navas-Carretero, S., Huttunen-Lenz, M., Taylor, M. A., Stratton, G., Swindell, N., Kaartinen, N. E., Lam, T., Handjieva-Darlenska, T., Handjiev, S., Schlicht, W., Martinez, J. A., Seimon, R. V., Sainsbury, A., Macdonald, I. A., Westerterp-Plantenga, M. S., Brand-Miller, J. and Raben, A. [2021]: 'A High-Protein, Low Glycemic Index Diet Suppresses Hunger but Not Weight Regain after Weight Loss: Results from a Large, 3-Years Randomized Trial', *Frontiers in Nutrition*, **8**, available at <doi.org/10.3389/fnut.2021.685648>.