Match and mismatch: conservation physiology, nutritional ecology and the timescales of biological adaptation

David Raubenheimer¹*, Stephen J. Simpson² and Alice H. Tait¹

¹Nutritional Ecology Research Group, Massey University, Albany, New Zealand
²School of Biological Sciences and the Charles Perkins Centre, The University of Sydney, New South Wales, Australia

Conservation physiology (CP) and nutritional ecology (NE) are both integrative sciences that share the fundamental aim of understanding the patterns, mechanisms and consequences of animal responses to changing environments. Here, we explore the high-level similarities and differences between CP and NE, identifying as central themes to both fields the multiple timescales over which animals adapt (and fail to adapt) to their environments, and the need for integrative models to study these processes. At one extreme are the short-term regulatory responses that modulate the state of animals in relation to the environment, which are variously considered under the concepts of homeostasis, homeorhesis, enantiostasis, heterostasis and allostasis. In the longer term are developmental responses, including phenotypic plasticity and transgenerational effects mediated by non-genomic influences such as parental physiology, epigenetic effects and cultural learning. Over a longer timescale still are the cumulative genetic changes that take place in Darwinian evolution. We present examples showing how the adaptive responses of animals across these timescales have been represented in an integrative framework from NE, the geometric framework (GF) for nutrition, and close with an illustration of how GF can be applied to the central issue in CP, animal conservation.

Keywords: nutritional homeostasis; nutritional ecology; geometric framework for nutrition; allostasis; conservation physiology

1. INTRODUCTION
As biologists, we live in privileged times. We ply our trade in an environment shaped by the conceptual contributions of intellectual giants—Charles Darwin, Claude Bernard, Niko Tinbergen, Ronald Fisher and Bill Hamilton, to mention just a few—while technological advances provide unprecedented opportunities for expanding and refining their legacies. This expansion has driven increasing overlap between conventionally defined research fields, providing further opportunity for conceptual advances to structure the emerging hybrid fields. A good example is the transformational contribution to evolutionary thinking that emerged from the intersection of behaviour, ecology and population genetics, in the field of Behavioural Ecology [1–4]. Other examples include Evo-Devo [5], Neuroethology [6], Ecological Immunology [7], Evolutionary Medicine [8,9], Cognitive Ecology [10] and, more recently, Pharmecology [11,12]. Most relevant in the present context, however, is the emerging field of Conservation Physiology (CP).

CP has an important goal of understanding the physiological responses of organisms to changed environments [13,14]. It draws on the techniques and concepts of physiology, and can in turn contribute to understanding how physiological systems mediate between capricious environments, animal fitness and ultimately population and community dynamics [15]. The aim is not merely to describe the patterns relating physiological responses to the environment, but to provide a detailed mechanistic understanding of the factors that cause conservation problems [13]. Another hybrid field, Nutritional Ecology (NE), also has similar aims. The overarching goal of NE is to unravel the extensive web of nutritional links that directs animals in their interactions with their ecological and social environments [16,17]. These links touch upon just about every aspect of biology, and their study draws on, and has the potential to contribute to, multiple research fields [18]. We believe that there are fundamental points of contact between CP and NE, and that both fields can benefit from an exploration of these.

Our aim in this paper is to examine and develop what we consider to be the principal points of contact between CP and NE. We do so by first presenting a view of how CP relates to a recently published conceptual scheme of NE [17] (§2). This comparison reveals...
strong isomorphisms between the fields, suggesting that there is significant scope for mutual enrichment. Key shared themes include the question of how animals respond to variation in their environments, and the adoption of an integrative approach for understanding these responses. In §3, we briefly review some of the concepts surrounding short-term, regulatory responses of animals to changing environments that are central to both CP and NE, from homeostasis to allostasis. The emphasis in both fields on adaptation and fitness requires consideration also of long-term, developmental, ecological and evolutionary responses, and these are the subject dealt with in §4. In §5, we introduce an integrative platform from NE, the Geometric Framework (GF) for nutrition, and present a number of examples showing how the responses of animals at different timescales to environmental variability have been represented within this framework. In §6, we consider the application of GF in the context of animal conservation, and briefly conclude in §7.

2. INTEGRATION, NUTRITIONAL ECOLOGY AND CONSERVATION PHYSIOLOGY

(a) Nutritional ecology—expanding the organism

The core components of NE are the organism, the environment and the nutrition-mediated interactions between the organism and environment. Raubenheimer et al. [17] depicted these interactions using a series of arrows, noting that those presented are a sub-set of a considerably richer reticulation of connections. To establish the common ground with CP, here we briefly expand one component of the scheme of Raubenheimer et al. [17], the organism (figure 1).

In the original version, the organism is depicted using categories similar to Tinbergen’s four levels of analysis: mechanism, development, function and history [19]. Rather than ‘history’, Tinbergen used the more specific term ‘evolution’, by which he meant ‘...the course evolution must be assumed to have taken, and the unravelling of its dynamics’ [20, p. 428]. Since 1963 it has become clear, however, that animals may be subject to other historical shaping influences at a timescale intermediate between Tinbergen’s ‘development’ and ‘evolution’, for example, transgenerational effects mediated by epigenetic mechanisms or broader mechanisms related to parental physiology and behaviour [15,21,22]. We have therefore used the general term ‘history’ to encompass transgenerational effects involving changes in gene frequencies (Tinbergen’s evolutionary history), as well as those mediated by epigenetic and related mechanisms. Given the tight continuity between developmental adaptation via phenotypic plasticity and non-genetic trans-generational adaptation (see §4), in figure 1 we have categorized Tinbergen’s ‘development’ as a short-term historical shaping influence.

An important aspect of the schematic organism in the present context is to distinguish between different categories of ‘mechanism’. Tinbergen did not, in fact, use the term ‘mechanism’, but rather referred to the ‘causation’ of behaviour. This enabled him to discuss some broader nuances of behavioural theory, for example the pitfalls of teleology (the attribution of purpose to animals): ‘Teleology can be said to have ceased to be a source of confusion in its cruder forms, in which function was given as a proximate cause, but it may well be a stumbling block to causal analysis in its less obvious forms’ [20, p. 301]. That aside, Tinbergen’s discussion of ‘causation’ very clearly made a distinction which in the present context is primary, that between the different levels of organization studied by ethologists and physiologists. Neurophysiologists of the time typically studied simple behaviours that could readily be ascribed to specific neural circuits, such as escape responses, whereas ethologists dealt with more complex behaviours that could not readily be partitioned into component physiological mechanisms but required analysis at the level of the ‘intact animal’ [20, p. 303]. The aim of ethologists was thus to partition the behaviour into its ‘behavioural’ components (e.g. ‘fixed action patterns’, ‘innate releasing mechanisms’, ‘motivation’, etc.), and build verbal or cybernetic models of how these fitted together.

---

Figure 1. Conceptual scheme depicting the common and distinctive features of Conservation Physiology (CP) and Nutritional Ecology (NE) (modified from Raubenheimer et al. [17]). In both fields the organism is considered from the viewpoints of function, mechanism, development and history [19], while the environment is partitioned into biotic and abiotic components. The interest in both fields on adaptation to changing environments warrants explicitly distinguishing the different timescales over which the environment influences phenotype (‘history’). In NE, the interactions of interest between organism and environment specifically involve nutrition, whereas CP has no such restriction. On the other hand, the focus in CP on physiology provides a more restrictive characterization of the organism than NE, which equally weights various phenotypic attributes (behaviour, physiology, morphology, life history, etc.). These are distinctions of emphasis only, since both CP and NE are richly integrative and regard multiple domains as necessary routes of enquiry for understanding the interactions between organism and environment.

---

Phlo. Trans. R. Soc. B (2012)
Tinbergen was characteristically clear on the relationship between the mechanisms studied by physiologists and by ethologists. First, he recognized that they form a continuum: ‘I believe that it is doing our science a great deal of harm to impose boundaries between it and Physiology where there are none, or rather where there is only a “cline” from behaviour analysis on the one extreme to “Molecular Biology” on the other’. (Note Tinbergen’s use of quotation marks around Molecular Biology, reflecting the then embryonic status of this influential scientific hybridization). Second, Tinbergen was optimistic that the two fields acknowledge that to understand these interactions it is often necessary to divert our gaze to a lower level of organization, and explore the individual-level traits that shape the interactions of animal and environment [14,17,23]

The fields differ to some extent, however, in emphasis. First, in NE the organism itself is represented by a slightly higher level of integration, which includes physiology as well as behaviour, morphology, life history and other phenotypic characteristics, whereas CP focuses more narrowly on the organism as physiology. Second, in accordance with its applied objectives, CP stresses the relationship between the organism and specifically those environments that have been altered by human activities [13,14], whereas the baseline for nutritional ecologists is the environment in which nutritional regulatory mechanisms evolved. A third point of difference is that in NE the link between organism and environment is more narrowly constrained to those points of contact that are mediated by nutrition, whereas CP involves no such stricture (figure 1).

These points of difference should not, however, be overstated. Both fields are broadly integrative, and the differences are to be found more in the starting point and emphasis rather than in the progression of research programmes. Thus, conservation physiologists take a high-level view of physiology, which provides an approximately complete model of the organism: ‘The physiology we are referring to usually includes whole-organism function such as metabolism, thermal relationships, nutrition, endocrine responses to environmental changes and changes in immune parameters’ [13, p. 38]. (This is strongly reminiscent of Tinbergen’s view of the level of behaviour that was the focus of interest for ethologists, discussed above). Furthermore, conservation physiologists necessarily include behaviour, morphology, and life history in their studies, because these provide the context within which physiological dynamics are linked to altered environments. For instance, the example of osmoregulation in desert tortoises provided by Wikelski and Cooke [13, p. 42] involves not only physiology, but also behaviour (food choice and drinking) and life history (hibernation). Likewise, nutrition touches on just about every facet of an animal’s life, and therefore provides a conduit for nutritional ecologists into many aspects of biology that are not conventionally considered ‘nutrition’ [18]. CP and NE are therefore fundamentally similar, and we believe that both would benefit from developing the common ground.

3. ADAPTING TO CHANGING ENVIRONMENTS: SHORT-TERM REGULATORY RESPONSES

Added to their integrative agendas, another important point of overlap between CP and NE is the shared community associated with a field. In this respect, namely the level of integration that provides the primary focus, NE and CP are closely related. In both fields, the principal focus is the interaction of the whole organism with its environment, and the outcome of primary interest is demographic (population sustainability and evolutionary fitness). And yet both fields acknowledge that to understand these interactions it is often necessary to divert our gaze to a lower level of organization, and explore the individual-level traits that shape the interactions of animal and environment [14,17,23].

The fields differ to some extent, however, in emphasis. First, in NE the organism itself is represented by a slightly higher level of integration, which includes physiology as well as behaviour, morphology, life history and other phenotypic characteristics, whereas CP focuses more narrowly on the organism as physiology. Second, in accordance with its applied objectives, CP stresses the relationship between the organism and specifically those environments that have been altered by human activities [13,14], whereas the baseline for nutritional ecologists is the environment in which nutritional regulatory mechanisms evolved. A third point of difference is that in NE the link between organism and environment is more narrowly constrained to those points of contact that are mediated by nutrition, whereas CP involves no such stricture (figure 1).

These points of difference should not, however, be overstated. Both fields are broadly integrative, and the differences are to be found more in the starting point and emphasis rather than in the progression of research programmes. Thus, conservation physiologists take a high-level view of physiology, which provides an approximately complete model of the organism: ‘The physiology we are referring to usually includes whole-organism function such as metabolism, thermal relationships, nutrition, endocrine responses to environmental changes and changes in immune parameters’ [13, p. 38]. (This is strongly reminiscent of Tinbergen’s view of the level of behaviour that was the focus of interest for ethologists, discussed above). Furthermore, conservation physiologists necessarily include behaviour, morphology, and life history in their studies, because these provide the context within which physiological dynamics are linked to altered environments. For instance, the example of osmoregulation in desert tortoises provided by Wikelski and Cooke [13, p. 42] involves not only physiology, but also behaviour (food choice and drinking) and life history (hibernation). Likewise, nutrition touches on just about every facet of an animal’s life, and therefore provides a conduit for nutritional ecologists into many aspects of biology that are not conventionally considered ‘nutrition’ [18]. CP and NE are therefore fundamentally similar, and we believe that both would benefit from developing the common ground.

Phil. Trans. R. Soc. B (2012)
interest in questions of how animals maintain their functional integrity in the face of environmental variation. This question has long been a theoretical focus in the physiological sciences, in which several models have been proposed to characterize the short-term dynamic physiological responses of animals to environmental perturbations. In this section, we briefly review the main concepts, and in the next section consider some of the long-term adaptive responses, which are most commonly considered in the context of life-history theory and evolution.

(a) Regulatory dynamics: homeostasis, feedback, homeorhesis, heterostasis and enantiostasis

An influential contribution to the development of theory surrounding an animal’s responses to varying environments was Claude Bernard’s concept of the ‘milieu intérieur’ (see [24] for an informative review). Bernard’s work, initially on digestion, then on carbohydrate storage in the liver, and especially on body heat, led him to observe that the ‘higher animals’ (by which he meant endothermic vertebrates) maintain internal stability in the face of environmental change. Bernard concluded that the regulation of body temperature is achieved through the neural integration of various physiological systems, including thermogenesis and the regulation of heat loss via vasomotor control [24]. His focus on thermoregulation, however, resulted in Bernard linking his principle too strongly with ‘higher animals’ (by which he meant endothermic vertebrates) maintain internal stability in the face of environmental change. Bernard concluded that the regulation of body temperature is achieved through the neural integration of various physiological systems, including thermogenesis and the regulation of heat loss via vasomotor control [24]. His focus on thermoregulation, however, resulted in Bernard linking his principle too strongly with ‘higher animals’, and underestimating its generality. As we shall see in §5, ectotherms such as insects, too show impressive feats of homeostatic regulation.

Among the many influenced by Bernard’s work were Scottish physiologist John Scott Haldane (father of J. B. S. Haldane, an important contributor to the Modern Synthesis in evolutionary theory) and Harvard physiologists Lawrence Joseph Henderson and Walter Cannon. Henderson’s work on the chemical buffering of the blood led him to make a much lower-level interpretation of Bernard’s ideas, attributing the constancy of the ‘milieu intérieur’ to physico-chemical processes. Haldane, who studied respiratory physiology, disagreed, and emphasized the importance attributed by Bernard to high-level coordinated compensatory responses to environmental changes. Not surprisingly, given his work on the coordination of physiological responses by the autonomic nervous system, Cannon supported Haldane in this. Indeed, Cannon went further and introduced the term ‘homeostasis’ to distinguish the coordinated physiological compensatory responses of interest to him and Haldane from the chemical equilibria that preoccupied Henderson. Cannon also elaborated on the concept of physiological compensation, stressing that homeostasis does not achieve a single fixed equilibrium state as do purely physico-chemical systems, but restricts the variation of physiological variables to a limited range. In so doing he shifted the emphasis in regulatory physiology from Bernard’s steady state (which is what he called ‘homeostasis’) to the physiological processes that buffer the internal environment from external changes (the ‘homeostatic mechanisms’).

Cannon’s emphasis on the mechanisms of homeostasis laid the foundation for his collaborators (Rosenblueth et al. [25]) to introduce into regulatory physiology the concept developed in military cybernetics of the ‘negative feedback’: ‘information that brings the output into closer proximity to the designated goal’ [24]. Rosenblueth et al. [25] highlighted the role of feedback not only in the self-limiting, homeostatic context, but also in predictive behaviour, a subject to which we return below. A third contribution of this paper was to define ‘teleology’ in mechanistic terms, thus initiating the process of purging it of the philosophical baggage to which Tinbergen referred in the quotation above. Pittendrigh [26] subsequently introduced the term ‘teleonomy’ in the hope of completing this process, although this was not altogether successful [27].

In the following decade, pioneering evolutionary developmental biologist Waddington [28] introduced the term ‘homeorhesis’ to describe dynamical systems in which the negative feedback effects a return to a trajectory, rather than to a ‘set point’ as in the Bernard–Cannon concept of homeostasis. For example, the regulatory processes that maintain physiological equilibrium during changes in nutrient demand with development, reproduction and scheduled changes in activity levels (e.g. for migration [29]) are homeorhetic. Other terms, including ‘rheostasis’, have been introduced to describe essentially the same concept [30].

An important variant on the concept of homeostasis was introduced by Hungarian endocrinologist Hans Selye [31,32]. Selye observed that in some cases physiological systems respond to externally imposed perturbations not by homeostatically restoring the status quo, but by adapting the regulatory set points to cope with the stressors. For example, an animal that is chronically exposed to high levels of xenobiotics might establish a new equilibrium where the tissues become tolerant and/or detoxification enzymes are chronically upregulated. Selye suggested the term ‘heterostasis’ to describe such altered regulatory equilibria. A significant contribution of this concept is the extension of homeostasis from short-term regulatory dynamics to encompass a longer time frame, in which the regulatory mechanisms themselves adapt to environmental perturbations.

Another extension of the time horizon of homeostasis was Moore–Edé’s [33] distinction between ‘reactive homeostasis’ and ‘predictive homeostasis’. Echoing the groundwork laid by Rosenblueth et al. [25], Moore–Edé suggested the term ‘reactive homeostasis’ to describe standard Bernard–Cannon homeostasis in which the animal compensates in response to environmental changes that have already occurred, contrasting this with ‘predictive homeostasis’ in which corrective actions are initiated in anticipation of a predictable environmental change. An advantage of this is that it enables the animal to avoid excessive uncompensated exposure to hostile environments in circumstances where the compensatory mechanisms take time to develop the required response—for example, where the synthesis of proteins is involved. Moore–Edé provides the example of diurnal primates in which raising the body temperature to optimal...
daytime levels takes over an hour, and consequently metabolic heat production, accompanied by coordinated changes in peripheral heat loss, is initiated in advance of dawn. As noted by Moore-Ede [33], a disadvantage of such anticipatory responses is that they can seriously compromise the animal's homeostatic integrity in cases where the prediction is incorrect. Although these ideas have not found widespread use in the physiological sciences, similar concepts have become established in relation to longer-term, developmental adaptation of animals to their environments. We will return to this in §4.

A critical contribution to homeostasis research was made by Curt Richter [34]. Richter studied engineering for three years in Germany, but eventually graduated from Harvard with an undergraduate degree in biological sciences. During his time at Harvard, Richter developed an interest in animal behaviour, and as a young graduate moved to Johns Hopkins University School of Medicine to do postgraduate research under the supervision of behaviourist psychologist John B. Watson. The confluence of engineering, Harvard (with its illustrious contributions to homeostasis research via Lawrence Joseph Henderson and Walter Cannon) and animal behaviour led Richter to develop an interest in the role of behaviour in physiological homeostasis. In his long and productive career (producing over 375 papers and spanning 60 years in the same laboratory), Richter performed a number of experiments demonstrating that rats could compensate for surgically induced perturbations to physiological regulatory systems involved in nutritional homeostasis by altering ingestive behaviour. For example, rats that were surgically induced by adrenalectomy to lose excessive amounts of sodium in the urine compensated by specifically increasing their intake of salt, and likewise surgically induced losses of calcium were compensated by increasing calcium intake. Richter also performed a series of experiments demonstrating that rats can self-select from a range of nutritionally incomplete foods a diet that contained the required amounts of nutrients. Although the interpretation of these experiments has been questioned [34], recent work on organisms from slime moulds to mammals confirms this for the energetic macronutrients ([18], see also §5).

Mangum and Towle [35] contributed a subtle but important elaboration on homeostasis, in the concept of 'enantiostasis'. Enantiostasis refers to cases where animals respond to perturbations in the environment not by maintaining the internal physical state (e.g. temperature, circulating glucose, etc.), but by maintaining the functionality of the system in the absence of homeostasis. An example is the sugar trehalose, which varies widely in the blood of insects and is thus not 'homeostatic' in the usual sense. However, this variation is essential for fulfilling the various functional roles of trehalose: an energy store, a cryoprotectant, a protein stabilizer during osmotic stress, and a component of a feedback mechanism regulating food intake [36]. The importance of the enantiostasis concept is that it shifts the emphasis in homeostasis from the maintenance of physical states (e.g. blood sugar concentrations) to functional outcomes, and in so doing takes physiology closer to a synthesis with the evolutionary sciences. The concept to which we now turn, 'allostasis', lays the ground for completing this synthesis.

(b) Allostasis

The dispute between Henderson on the one hand, and Haldane and Cannon on the other was at base a debate over the level at which physiologists should integrate the self-correcting properties of physiological systems. Henderson saw the regulation of pH resulting from interactions among blood-borne chemicals, whereas Haldane and Cannon saw homeostasis arising from the integrated outputs of higher-level physiological systems, such as energy metabolism and vasomotor control. Curt Richter expanded the integrative scope of homeostasis further to encapsulate behaviour, while Selye's 'heterostasis' [32] and Mangum and Towle's [35] 'enantiostasis' emphasized long-term responses and functional considerations, respectively. Allostasis represents an even broader synthesis, which provides a framework for integrating and expanding the various developments on the concept of homeostasis discussed in the previous section.

The model of allostasis [37,38] distinguishes between those systems, such as body temperature, pH, oxygen tension and glucose levels, which need to be maintained within tight limits to sustain life ('homeostasis'), and other supporting systems that have a more adaptable operating range and help in buffering the homeostatic variables against perturbations ('allostasis'). Ostensibly, this distinction represents a higher level of integration than models based on the homeostatic system alone, because it broadens the view to encompass both the primary and supporting systems. As noted by Day [39], however, there is a fine line between this and the Bernard–Cannon model discussed above, where homeostasis is seen as the outcome of the coordinated activities of several responses (e.g. thermogenesis and vasomotor control), because the Bernard–Cannon model also encompasses supporting systems (e.g. vasomotor control). Nonetheless, the emphasis in allostasis on the role of the brain as a central coordinator of the response of the entire organism [40] to stressful circumstances suggests a significant difference in degree, if not in kind, in the level at which allostasis integrates organismal responses compared with the homeostasis model.

In important respects, however, this distinction of degree crosses a threshold where categorical differences between the models emerge. For example, the high-level view of the response of animals to changing environments in the allostatic model opens the way for considering dimensions of the environment that do not directly relate to classic homeostatic systems, for instance predator avoidance and social stressors such as competition for status and mates [38,41,42]. It also provides a framework in which to consider broader responses of animals to stressors, such as alterations to the life cycle [38].

An aspect of the allostasis model that is particularly important in the present context is its recognition that to maintain the status of the defended outcome, the supporting systems are often perturbed—for example,
elevated heart rates might in a particular circumstance be required to maintain the delivery of oxygen and glucose to cells [38]. This by itself is not different from Cannon's perception of homeostatic systems [39], but the crucial addition is the explicit realization that depending on the magnitude and persistence of the environmental change, these perturbations might extend the supporting systems beyond their optimal operating range and incur fitness costs. The term 'allostatic load' describes the cumulative results of sustained perturbations to the supporting systems, which beyond a critical threshold becomes a costly 'allostatic overload'. The consideration of fitness costs opens the way for the important integration, central both to CP and NE, between phenotype (in this case physiological dynamics) and Tinbergen's functional question of how the animal benefits from the phenotype.

In a slightly different formulation (see also [43] for a comparison of the two), the concept of allostasis is even more explicit about the link between structure and function in physiological systems. Peter Stirling, one of the originators of the allostasis concept, stresses the adaptive nature of allostatic systems. To Stirling [41], an allostatic system is a system in which the set points for internal states are not static points as in homeostasis, or even trajectories as in homeorhesis, but shift in response to environmentally imposed perturbations. (In this respect Stirling's model closely resembles Selye's concept of heterostasis, discussed above). Initially there are costs to the system of functioning outside of its normal operating range, for example, reduced efficiency and sensitivity, but if the deviation is prolonged, then the system adapts to centre itself in the new operating range and reduces the costs by restoring efficiency and sensitivity. In this formulation, physiological systems are self-correcting not in the classic homeostatic sense of defending a specific internal state (e.g. temperature), but in the sense that they adjust their structure to maintain functional optima (e.g. efficiency and sensitivity). Furthermore, not only are allostatic systems reactive in adapting to perceived environmental changes but, recalling Rosenblueth et al. [25] and Moore-Ede's [33] 'predictive homeostasis', they also adapt to anticipated changes in future demand.

In the present context, the most important point about Sterling's formulation is that it stresses function rather than state, recognizing that the goal of regulation is 'not constancy, but rather fitness under natural selection' [41]. This statement is reminiscent of Mangum and Towle's [35] concept of enantiostasis, except that it transcends individual functional outcomes such as adequate energy stores and osmotic equilibrium, referring to the totality of these and thus to the variable that is ultimately 'regulated' in biology, evolutionary fitness.

Under the concept of allostasis, animals can thus be viewed as a set of physiological and behavioural components whose interactive function is to maximize evolutionary fitness (rather than maintain a particular state such as blood glucose), where each component may incur both benefits and costs. This opens the way for incorporating into models of physiological dynamics the important economic concepts of evolutionary biology, through exposing to scrutiny the matrix of cost–benefit trade-offs that link the different components of regulatory systems. One advantage of this is that it draws attention to optimal design criteria. Sterling [41], for example, discusses six interrelated design criteria that underlie allostasis: (i) organisms are designed for efficiency; (ii) efficiency requires reciprocal trade-offs; (iii) efficiency requires predicting what will be needed; (iv) prediction requires each sensor to adapt its sensitivity to the expected range of input; (v) prediction requires each effector to adapt its output to the expected range of demand; and (vi) predictive regulation depends on behaviour whose neural mechanisms also adapt. At a higher level, the economic focus exposes for analysis the net benefits to the animal of inhabiting its evolutionarily adapted environment, the costs associated with perturbations to the conditions of this environment, and the scope and mode of adaptive responses that these perturbations elicit. These net benefits, costs and adaptive responses occupy the central ground of overlap between CP and NE.

4. ADAPTING TO CHANGING ENVIRONMENTS OVER THE LONGER-TERM

The Bernard–Cannon concept of homeostasis (reactive homeostasis) concerns short-term adaptive regulatory responses of animals to environmental perturbations. The time frame is extended to some extent in predictive homeostasis, where animals compensate in advance for anticipated future environmental changes, and even more so in heterostasis and allostasis, where prolonged exposure to stressors results in adaptive shifts in the parameters of the regulatory systems. In this section, we briefly introduce a number of concepts from outside of the physiological literature that have been developed to model the ways that animals respond over longer timescales to environmental variation.

(a) Phenotypic plasticity

The adaptive shifts in the regulatory targets of heterostasis and in the operating ranges of allostatic systems discussed above represent a form of phenotypic plasticity in which an individual organism can change its phenotypic state in response to variations in environmental conditions [44]. A second form of phenotypic plasticity involves the possibility to modify developmental trajectories in response to environmental cues [44]. A definition of phenotypic plasticity that encompasses both of these categories is 'the ability of individual genotypes to produce different phenotypes when exposed to different environmental conditions' [45].

Mayr [46] used a term coined by C. D. Michener, 'polyphenism', to describe intraspecific variation that results from phenotypic plasticity, to differentiate it from intraspecific variation with a genetic basis (termed 'polymorphism'). Mayr's use of polyphenism was broadly based, encompassing discontinuous and continuous phenotypes, those present within as well as between developmental stages and seasons, fixed and reversible phenotypic states, and adaptive traits as well as those apparently offering no selective advantage [47,48]. Other definitions have been more restrictive, and polyphenism is now often recognized
as a particular case of phenotypic plasticity, in which two or more distinct phenotypes (without intermediates) are elicited by an environmental cue [49]. Whether discrete or continuous, the pattern of phenotypic variation that is produced by a single genotype across a range of environments is known as a ‘reaction norm’ [50,51].

When the effect of the environment on phenotypic plasticity is indirect rather than serving as a direct trigger, the conditions that induce the phenotype do not need to be the same as those to which the phenotype is an adaptation [52]. This provides scope for a time delay between the eliciting cue and the phenotypic response, where the cue can serve as a predictor of forthcoming environmental changes [53]. This concept is embodied in the ‘environmental mismatch hypothesis’ [54–56] and the related ‘predictive adaptive response’ (PAR) hypothesis [56,57] developed in the biomedical science literature in relation to the maintenance of human health and the origins of disease. In these models, changes that take place in response to environmental cues during development involve the juvenile preparing for the predicted adult environment to confer an advantage later in life. However, if the anticipated and realized adult environments are widely discrepant, the developmental responses may impose specific costs in the adult environment and the animal will be maladapted. This is suggested to be the case for many humans as a result of the recent worldwide nutritional transition to more energy-dense diets, the costs in this case being an increased risk of metabolic disease [58]. There are obvious parallels between these developmental concepts and the physiological predictive homeostasis model of Moore-Edes [33] discussed in §3, according to which corrective actions initiated to ameliorate anticipated environmental changes impose costs if the prediction is wrong.

(b) Transgenerational non-genetic inheritance

When an organism modifies its developmental trajectory for future benefit, the risk of a mismatch between the anticipated and realized environments can be mitigated by basing the response not only on the prevailing environmental conditions, but on the conditions experienced by recent ancestors. This information can be transmitted to a developing organism via non-genetic inheritance, which is defined as ‘any effect on offspring phenotype brought about by the transmission of factors other than DNA sequences from parents or more remote ancestors’ [22, p.106]. Non-genetic inheritance can thus be viewed as a form of plasticity that spans generations [59].

There are various mechanisms of non-genetic inheritance. Foremost in the recent literature is the transmission of variant epigenetic states (‘epialleles’), which occurs when variation in the epigenetic state of a parent or ancestor is maintained in the germline and transmitted to offspring [60]. Parental environment can also affect offspring phenotype through the transmission of cytoplasmic or somatic factors (e.g. hormones), or through the transmission of nutrients that can influence offspring condition and life history [22]. Transgenerational transmission of the extraorganismic environment may also occur, for example, when eggs or juveniles are deposited by a parent in a certain environment [22,61] or when behaviour is culturally transmitted across generations [22,62]. In §5, we discuss an example from NE where non-genetic transgenerational inheritance is important, while an example from CP is discussed in [15].

(c) Transgenerational genomic adaptation: Darwinian evolution

Over the long-term—usually several generations or more—gene pools adapt to environments through changes in gene frequencies driven by Darwinian evolution. The targets of natural selection include all of the adaptive mechanisms discussed above, from reactive homeostasis to transgenerational non-genetic adaptation. In other words, Darwinian evolution drives not only the adapted state of animals, but also their adaptive capacity.

Considerable challenges remain, however, in integrating gene-level evolution with the non-genetic transgenerational adaptation discussed in the previous section. This is because the prevailing accepted version of evolutionary theory, that of the Modern Synthesis, holds ‘the assumption that inheritance is the transmission to one’s offspring of DNA sequences received from one’s parents—a seamless genetic lineage all but impervious to external influences and perturbed only by rare mutation events . . .’ [22, p.104]. In the wake of empirical evidence for the occurrence of non-genetic mechanisms of inheritance, evolutionary theory is currently undergoing an intense period of discussion and re-evaluation, including a proposal for an ‘Extended Synthesis’ for evolutionary biology to accommodate (among other things) the phenomenon of non-genetic inheritance [63]. CP and NE are both fertile grounds for relevant examples, and would derive considerable benefit from this integration.

5. A VIEW FROM NUTRITIONAL ECOLOGY

Three central themes emerge from the preceding sections: (i) animals adapt to changing circumstances over multiple timescales, including behavioural and physiological responses, phenotypic plasticity and short and long time frame transgenerational adaptation; (ii) these adaptive dynamics are best understood using models that integrate across a broad range of biological attributes, drawing links between physiological systems, behaviour, development, life history and ultimately evolutionary fitness; and (iii) since CP and NE share a common mandate to understand the dynamic relationships between animals and their environment, both fields must draw on the concepts of adaptation developed in diverse disciplines including physiology, behaviour, life-history theory and evolutionary theory.

NE faces particular challenges (and opportunities) in this regard, since the specific focus on the nutritional links of animals and their environments calls for models that express the various components of these links (animal, environment and the adaptive responses of animals) in common terms, namely the salient nutritional currencies and their relationships with...
Darwinian fitness. The integrative work of such models is to interrelate these components and understand how the coordinated behavioural, physiological and developmental responses of animals mediate between environmental challenges and Darwinian fitness. Historically, the chosen currencies have been one dimensional, typically energy or nitrogen [17], or occasionally specific micronutrients that are considered to be limiting factors in the relevant circumstances (e.g. calcium [64]). In recent years, however, it has become clear that nutrients interact in complex ways in their effects on animals, and to understand these effects multidimensional nutritional models are needed [17,18].

In the remainder of this paper, we present a modelling approach from NE, called the Geometric Framework (GF) for nutrition, which has been developed to represent in the context of multiple nutrients the dynamic interactions of animals with their environments. In this section, we provide examples to demonstrate how the adaptive responses of animals over multiple timescales have been represented and interrelated within these models. We show how we have drawn heavily on the concepts from other disciplines discussed above (physiology, behaviour, life-history theory and evolutionary biology), and hope that our attempts to bring these together within a single framework might in turn offer some inspiration to those fields and to the integrative endeavours of CP.

In the final section, we provide examples where this approach has been applied specifically in the context of conservation biology. The conceptual basis of GF has been reviewed several times, and rather than repeat that here we refer readers to the relevant literature [17,18,65–68].

(a) **Homeostasis**

A central conceptual element in GF nutritional models is that of regulatory targets. These represent ideal points of nutrient intake and allocation for growth and development, target points are represented within multi-dimensional nutrient spaces. Numerous experimental studies using GF designs have demonstrated that organisms ranging from acellular slime moulds [69] to mammals [70,71] regulate their intake of multiple nutrients to an intake target when experimentally challenged with perturbations to their nutritional environment or nutritional state (reviewed in [18]). Two striking examples from insects are presented in figure 2.

How do animals achieve these remarkable regulatory feats? The task required of the regulatory systems controlling nutrient intake is to assess the composition of available foods in relation to the current nutritional state of the animal and to direct feeding responses appropriately to achieve the intake target [18]. Peripheral nutrient sensors on external appendages, within the mouth, and along the gastrointestinal tract detect key aspects of food composition before, during and after ingestion. Not all required nutrients are sensed directly, however. Rather, a subset of key nutrients is detected, usually comprising salts, sugars and amino acids [74]. Learned associations between non-nutritional food cues and the post-ingestive consequences of ingesting those foods offer extra means of detecting limiting or harmful excesses in foods of nutrients not directly detected by gustatory receptors [75–79].

Assessing current nutritional state involves the animal monitoring changing levels of key nutrients and their metabolites in the circulation, as well as

---

**Figure 2.** Results from two experiments demonstrating regulation to a protein:carbohydrate intake target. (a) Locusts (*Locusta migratoria*) given one of four food pairings (%protein:%carbohydrate, 14:28 or 7:14 and 28:14 or 14:7) reached the same point in nutrient space by altering the amounts of the two foods eaten (data from Chambers *et al.* [72]). The open squares indicate the expected outcome if there was no homeostatic regulation of macronutrient intake. (b) Female German cockroaches (*Blattella germanica*) were confined for 48 h to one of three nutritionally imbalanced foods (the dashed lines). The first point in each series (i.e. that closest to the origin) shows the bivariate mean for the amounts of protein and carbohydrate eaten across this pretreatment period. Subsequent points in each series represent cumulative intakes after a further 4, 10, 24, 48 and 120 h in which the insects had access to all three foods simultaneously and could move freely within the nutrient space (after Raubenheimer & Jones [73]).
chemical signals emanating from nutrient stores and body reserves [80,81]. Therefore, perturbations in the objects of homeostasis (nutrients) are themselves regulatory signals. Information about nutritional state and food composition converge and are integrated by neural pathways controlling appetite and feeding behaviour, including the peripheral gustatory receptors [82] and central circuitry in the brain [83,84]. Within this integrative circuitry is an embodiment of the target state of the animal: hence, for a given disparity between food composition and current nutritional state, the solution to reaching the intake target will be represented in the output of the neural circuits controlling appetitive behaviour.

Once nutrients are ingested, post-ingestive regulation occurs at multiple stages to achieve homeostatic regulation of growth and metabolism. Even if the animal is constrained from reaching its intake target, regulation of growth and body composition can be achieved by regulatory adjustments to nutrient digestion and absorption [85], metabolism [86,87] and excretion [88] (figure 3).

(b) Homeorhesis
While nutritional targets can be considered as multidimensional points of homeostasis when integrated across a given time period, consistent with Waddington’s definition of a homeorhetic system, they can also be represented as dynamic trajectories which move through nutrient space over time in response to changing environmental conditions (e.g. temperature), shifting physiological and behavioural demands, and developmental stage (figure 4) [18,67,68]. The functional challenge facing an animal is, therefore, to track a moving intake target in multidimensional nutrient space.

Lifestage-specific shifts in nutritional regulatory mechanisms and their targets can be set as part of the developmental programme (non-demand-driven, sensu [92]), or else achieved as a result of shifting demands for nutrients at different lifestages acting via an unchanging, common regulatory system (demand-driven, sensu [92]). For example, the rapidly induced preference for protein-rich yeast in female Drosophila after mating results not from depletion of protein reserves as eggs are developed (a demand-driven response), but as a direct result of a sex peptide that is introduced with the male’s seminal fluid during mating and stimulates specialized sensory neurons in the female’s reproductive tract. An additional demand-driven mechanism then modulates how much yeast is eaten, involving TOR/S6 kinase and serotonin signalling pathways in the central nervous system [93,94].

(c) Allostasis
Optimal nutrition involves an animal acquiring a particular blend of nutrients from its environment at an appropriate rate. This can readily be achieved by selecting a balanced food—i.e. one that contains the nutrients in the same proportion as they are required by the animal—or by mixing their intake from nutritionally complementary foods [67,68] (target selection—see figure 2 for examples). However, where the animal feeds on non-complementary imbalanced foods it cannot balance its intake of all nutrients, but is constrained to over-ingest some nutrients and/or under-ingest others. In this situation, a hierarchy of
nutritional priorities determines which nutritional requirements are satisfied, and which are under- and which over-ingested. This is analogous to the allostatic model, where some physiological systems are homeostatically defended at the cost of perturbations to others (the allostatic systems). Failure to achieve the target intakes for the ‘allostatic’ nutrients engenders fitness penalties [18,95], where the accumulated costs associated with being off-target are directly analogous to the concept of allostatic load. In the GF these ingestive trade-offs are termed ‘rules of compromise’ [65,67], and are measured by confining animals to one of a range of dietary compositions and describing the shape of the resulting nutrient intake array (figure 5).

Rules of compromise are an important parameter of nutritional regulation, and consequently adapt over various timescales to environmental circumstances. Not surprisingly, therefore, diverse examples have been described. In some cases animals on imbalanced diets abandon intake regulation of some nutrients to defend the target for others. For example, locusts will regulate their intake of salt and macronutrients to an intake target if allowed to select between nutritionally complementary foods, but defend macronutrient intake and abandon salt regulation when confined to diets of fixed composition [97]. In other cases, the trade-off is not so one-sided, with the animal accepting an intermediate compromise where more moderate excesses of some nutrients are combined with deficits of others. Two examples of this are given in figure 5, comparing the rule of compromise for protein and carbohydrate in a nutritional specialist and a generalist grasshopper. When confined to nutritionally imbalanced foods both species over-ate the surplus nutrient as well as under-ate the deficient one, but the generalist showed a greater capacity to ingest surpluses than did the specialist. This comparison is discussed further in §5e below.

(d) Cost–benefit analyses

The shapes of rules of compromise embody the relative fitness costs of ingested excesses and deficits [95]. Some of these costs are direct physiological consequences, but others reflect anticipated ecological costs such as the probability over time of having to endure nutritional imbalances before nutritionally complementary resources are contacted (see below). By confining animals to one of a wide range of nutrient intakes and measuring the associated performance consequences, it becomes possible to use surface-fitting methodologies to infer the shape of fitness landscapes and then to measure the extent of alignment between regulated points of intake and compromise arrays. An illustration is provided in figure 6. Here, female predatory carabid beetles were confined to one of 25 diets differing systematically in the concentration and ratio of protein and lipid. A response surface was constructed based on the numbers of eggs developed by the beetles. When allowed to select among complementary foods, beetles mixed a diet that aligned with the peak on the egg production landscape. If confined to one of 10 diet compositions that did not allow the peak to be reached, beetles ingested the amount of food needed to reach the highest available egg production for that dietary protein to lipid ratio [98]. Were the regulated intake target or the rule of compromise array not to have aligned with the underlying egg production landscape, it would have implied either that the landscape did not capture one or more key aspects of Darwinian fitness, or that there was a mismatch between the beetles’ evolved regulatory mechanisms and the nutritional environments tested [18,95].

Surface methodologies also provide a powerful device for comparing cost–benefit analyses across different response variables. One example has been their use...
in exploring the relationship between lifespan and reproductive effort in *Drosophila* and other insects [99–101]. Lee et al. [99] confined mated female flies to one of 28 diets varying in protein and carbohydrate content. The resulting surfaces for lifespan indicated that flies lived progressively less long as the ratio of protein to carbohydrate in the diet rose above 1 : 16. This showed that, contrary to widespread consensus, nutrient balance rather than caloric intake determined lifespan—a conclusion supported by studies on other insects and also suggested by existing data on mammals [102].

When a surface was constructed for lifetime egg production, the peak lay at a higher protein to carbohydrate ratio (1 : 4) than supported maximal lifespan. When offered different pairs of complementary foods, flies unerringly mixed a diet with a 1 : 4 protein to carbohydrate ratio, thus indicating that their regulatory responses were attuned to achieve maximal lifetime reproductive output rather than maximal longevity.

Surface methodologies have recently been used to consider nutritional trade-offs among another class of response variables: components of the innate immune system. Cotter et al. [103] confined caterpillars to one of 20 diets differing in protein and carbohydrate content and found that different immune components had differently shaped response surfaces with respect to macronutrient intake (figure 7). These surfaces provide an alternative to the prevailing assumption in both life-history theory and immunology that trade-offs are mediated by competition for energy or some other limiting resource [18,104]. Instead, GF analyses show that there are conflicting multi-nutritional demands between different life-history traits and between components of the immune response, and thus no one

Figure 6. Response surface plotting egg content in 500 mated female ground beetles, *Anchomenus dorsalis*, fed one of 25 diets varying in protein and fat content. The mean (± s.e.) lipid and protein intakes of the beetles that were allowed to compose their diet from two nutritionally complementary foods is plotted on top of the landscape in white. Nutrient intakes of beetles provided with ad libitum access to only one of the 10 foods are plotted on top of the landscape in black (mean ± s.e.) (after Jensen et al. [98]).

Figure 7. Response surfaces showing the effects of protein and carbohydrate eaten by uninfected *Spodoptera littoralis* caterpillars on two components of the innate immune system, (a) lysozyme activity (associated with fighting microbial pathogens) and (b) phenoloxidase activity (part of the encapsulation response to invading organisms). The two immune traits have very different landscapes in relation to macronutrient intake (after Cotter et al. [103]).
diet simultaneously maximizes all response variables. Consequently, the performance landscape that best reflects Darwinian fitness will depend on the animal's ecological circumstances, including its likelihood of dying early from predation, or its likelihood of being infected with particular diseases.

This raises the prospect that animals may be able to adjust diet choices to reflect shifts in their ecological circumstances. One example of such a response is nutritional self-medication in caterpillars [12,105,106], in which insects infected with either a bacterium or a virus selected a diet that was higher in protein than would normally be optimal, but which protected against infection. Whether insects are able to adjust their food selection behaviour to support specific immune components which best fight a particular infection remains to be seen [107]. There are numerous other examples of dietary self-medication to ameliorate the effects of disease and parasitism and to counteract ingestion of toxins [12].

(e) Adaptation over longer timescales

When the animal experiences a discrepancy between its current and target states, a regulatory response is evoked. The form, strength and nature of this response depend on the nature of the environment and the time for which the perturbation persists. Adaptive feedbacks to environmental changes operate over different timescales. Above, we have considered perturbations occurring both in the short term, which evoke physiological and behavioural regulatory responses to attain targets and rules of compromise, and across developmental time as targets move to track changing demands for growth, development and reproduction. Targets and rules of compromise also track changes in the nutritional environment that persist for longer periods, including across generations. These require more persistent phenotypic regulatory responses than short-term physiological or behavioural adjustments. Some such responses involve developmental plasticity, others are mediated by epigenetic adjustments that are transmitted across generations, and ultimately, phenotypes evolve via selected genetic changes.

A simple example is provided by an animal that encounters foods of different nutrient densities. The initial response is to prefer concentrated over dilute foods, as predicted by optimal foraging models assuming maximization of the rate of energy acquisition [108]. However, when only dilute foods are available, animals will over time this typically begin to eat these in greater amounts—a compensatory response that ensures regulation of the rate of nutrient acquisition. Hence, short-term nutrient maximization has shifted to long-term regulation. If a nutritionally dilute diet persists, then behavioural compensation may be accompanied by changes such as physical restructuring of the alimentary canal to increase the capacity for bulk throughput of dilute food [109,110]. If these responses fail to maintain nutrient supply, associated fitness costs will direct evolution of new phenotypes better able to manage a dilute diet. This same principle applies when food is distributed heterogeneously in space and time, with periods of availability being separated by extended periods without food. Here, the compensatory response is to eat more when food is available and have increased storage capacity to tide the animal over during periods of food shortage. Mechanisms include learning to eat bigger meals (conditioned satiety [111]), increased gut capacity and expanded fat depots.

As discussed in §2c, the shapes of rules of compromise are expected to reflect both direct costs of ingesting excesses and deficits of nutrients relative to the intake target, as well as anticipated ecological costs such as the probability of encountering nutritionally complementary resources. The probability of encountering complementary foods would be expected to vary with the mobility and diet breadth of an animal [68,112]. If an animal encounters a nutritionally imbalanced food, it must decide how much, if any, of that food to eat before moving on. The more that is eaten of the food, the smaller the shortfall in limiting nutrients, but the greater the excesses ingested of other nutrients and toxins. These excesses could prove costly [113] unless the animal subsequently encounters a complementary imbalanced food, in which case the potential cost of excesses will translate into a greater total intake of a balanced mix of nutrients. This probability would be expected to be higher for generalist feeders than for food specialists, leading to the prediction that generalist feeders should be more willing to over-consume imbalanced foods than would specialist feeders. In support of this prediction, evidence suggests that food plant generalist insect herbivores are indeed more willing to consume greater amounts of nutritionally imbalanced diets than matched food plant specialists [96,112,114–117] (see also figure 5).

Such shifts in ingestive strategies with diet breadth occur across evolutionary time, as indicated by cross-species comparisons [96,114–117] but they also can change via epigenetic effects. This was shown in a study on the desert locust, Schistocerca gregaria, which expresses density-dependent polyphenism. When reared under crowded conditions, Schistocerca nymphs develop into the swarm-forming gregarious phase, but if reared alone, nymphs develop into the solitary form, which displays camouflaged, green or brown coloration, avoids other locusts, and is much more sedentary in its behaviour [118–120]. Solitary locusts live in habitats that are dominated by a small number of host plants and are much more sedentary than gregarious-phase locusts. This means that solitary locusts should encounter lower nutritional heterogeneity than their much more mobile, highly polyphagous, gregarious counterparts [112]. Experiments showed that the two phases had the same protein–carbohydrate intake target, but that solitary-phase insects under-ate imbalanced diets compared with gregarious counterparts, as predicted by their ecology and behaviour. When locusts were in transition towards the solitary condition, having been reared in isolation from eggs laid by crowded-reared parents, they developed an intermediate response. These data provide strong evidence for epigenetic inheritance of the rule of compromise, as for other phase-related traits [120–122].
A compatible prediction is that generalists should better be able to deal with excesses post-ingestively. This was confirmed in studies of insect herbivores [96,112,114–117]. In each instance, generalists were better able than specialists to use excess ingested protein on high-protein, low-carbohydrate diets for energy metabolism, thereby simultaneously reducing the cost of surplus ingested protein and offsetting the carbohydrate deficit [96,115]. Over the eight generations, caterpillars from the high-protein environment progressively laid down more body fat per intake of carbohydrate (upwards grey arrow), while the opposite occurred under high-carbohydrate environments (downward grey arrow). Adapted from Warbrick-Smith et al. [124].

In addition to rules of compromise, evolved changes in intake targets have also been described. For example, Simpson and Raubenheimer performed a phylogenetically controlled comparative analysis of the position of the intake target in 117 insect species [123]. The analysis showed that insect species that are associated with mycetocyte symbionts have a significantly lower proportion of protein in the target diet than other insects. This is consistent with a role for mycetocyte symbionts in improving the nitrogen efficiency of their hosts.

In addition to rules of compromise, evolved changes in intake targets have also been described. For example, Simpson and Raubenheimer performed a phylogenetically controlled comparative analysis of the position of the intake target in 117 insect species [123]. The analysis showed that insect species that are associated with mycetocyte symbionts have a significantly lower proportion of protein in the target diet than other insects. This is consistent with a role for mycetocyte symbionts in improving the nitrogen efficiency of their hosts.

While the above analysis did not directly compare the protein utilization efficiency of the insects involved, post-ingestive responses have in other contexts been shown to adapt across generations to persistently changed environments. This was illustrated by Warbrick-Smith et al. in their study of the diamondback moth, Plutella xylostella [124]. Lines of P. xylostella were reared for a total of eight generations either on a carbohydrate-rich diet or a protein-rich diet. The carbohydrate-rich diet comprised either chemically defined artificial food (12% protein and 40% carbohydrate) or a high-starch mutant of the plant Arabidopsis. Over the eight generations, caterpillars progressively developed the ability to ingest excess carbohydrate without laying it down as body fat (figure 8), a result which provided strong evidence that storing excess fat has fitness costs. Other replicate lines of caterpillars were reared for eight generations in a protein-rich, carbohydrate-scarce environment, comprising either artificial diet (45% protein, 7% carbohydrate) or a low-starch Arabidopsis mutant. In contrast to insects reared under a high-carbohydrate environment, these caterpillars developed an increased propensity to store ingested carbohydrate as fat. Female moths also developed a preference for laying their eggs on the low-starch plant, whereas those selected on the high-starch Arabidopsis mutant showed no preference. It was not determined whether these changes in physiology were the result of genetic selection or accumulating epigenetic effects.

(f) Prediction

Like the models of predictive homeostasis and allostasis, NE recognizes the importance of both reactive as well as pre-emptive adaptation to changing environments. The intake target and its regulatory mechanisms embody demands for nutrients to supply the animal’s immediate needs, as well as any extras required to cover inevitable wastage during the transformation from ingestion to ultimate use [125]. Additional to these is some component of anticipated needs, which requires that the regulatory mechanisms include a
prediction of the future changing relationship between the animal and its environment—in other words, a nutritional feed-forward mechanism [126].

Some future changes in the relationship between an animal and its environment are highly predictable. On the animal side, these include inevitable changes in nutritional needs with development, reproduction and ageing (as discussed in §2b). It may also be possible to predict environmental changes with high accuracy, notably those associated with geophysical cycles [35]. Increased food intake, food caching and fat storage leading up to winter hibernation is one example, as is increasing fat reserves prior to seasonal migration. Other predictions are more probabilistic, based on sources of evidence from the past. These include the animal’s own recent and early-life experiences as mediated via learning and developmental switches, inferences from peers (social learning), parents and grandparents (epigenetic effects, cultural transmission, etc.), and the accumulated experiences of ancestors expressed through genetic evolution.

Present conditions may offer clues about the future, such as when high population densities presage impending food shortages and trigger the development of alternative nutritional phenotypes [48]. As discussed in §4, these are known as ‘PARs’ [57,127], and are typically shaped by associations experienced in ancestral environments. Problems arise, however, when the predicted environment fails to materialize: when there is a mismatch between prediction and reality.

MISMATCH

Mismatch occurs when the timescale and/or magnitude of environmental change exceeds the combined capacity of adaptation owing to homeostatic mechanisms, phenotypic plasticity and transgenerational adaptation. The example of the diamondback moth discussed in §2c above offers an illustration. By becoming less prone to laying down body fat in a high-carbohydrate world, P. xylostella caterpillars minimized the costs of obesity—but at the risk of starving for want of energy reserves if food became scarce. By contrast, in a low-carbohydrate world, retaining and storing carbohydrates as fat was favoured; but should such a phenotype be placed into a high-carbohydrate world it would be at risk of obesity [124].

As discussed in §4, the special case of mismatch in which a prediction about the future environment is wrong has been proposed to lie at the heart of the pandemic of metabolic disease facing humanity across much of the developed and developing world [128,129]. Experiments and meta-analyses [130–132] examining the rule of compromise for humans eating foods that have a protein density lower than the target density is to ingest the target level of protein while over-eating non-protein energy. The obvious implication of this, namely that humans are vulnerable to energy over-consumption in low-protein nutritional environments, has led to the suggestion that the current obesity epidemic stems from a mismatch between the human rule of compromise, which evolved in association with a high-protein diet [133], and the trend in modern diets towards reduced protein density e.g. [134]. This idea, known as the ‘protein leverage hypothesis’ of human obesity [131], is also consistent with the effectiveness of high-protein weight loss diets [135].

6. CONSERVATION NUTRITION

The concept of nutritional mismatch characterizes an important dimension in conservation: when the magnitude of environmental change exceeds the adaptive capacity of organisms, or the costs of adaption are excessively high, then conservation measures will be needed to improve the match between phenotype and environment. These might in some cases involve directly altering the organism, for example, through immunization programmes. In many cases, however, the environment is the target of management, for example, in predator removal programmes, the use of supplementary feeding and species translocations. Whatever the management strategy, it requires an understanding of the relationship between the animals’ habitat needs, the capacity of the environment to provide for these, and the responses of the animal to constraints on the ability to satisfy its requirements. Nutritional geometry offers a powerful approach for investigating these relationships.

For example, as discussed in §5, characterizing the rule of compromise in macronutrient regulation by humans has provided new insights into the consequences of mismatch between evolved nutritional regulatory systems and modern environments. Although no equivalent study has been done in the context of conservation, we have made a start by measuring the responses of two endangered primates to variation in the composition of naturally encountered foods in the wild. Felton et al. [136,137] combined field observations with laboratory analyses of food compositions to estimate the intake target of Peruvian spider monkeys (Ateles chamek) and test the responses of these primates to natural variation in food composition. Geometric analysis showed that the monkeys held protein intake considerably more constant than non-protein energy, thus showing a rule of compromise similar to that described for humans (figure 9). Rothman et al. [138] reanalysed previously published data [139] using GF to address the same questions for free-ranging mountain gorillas in Bwindi, Uganda. The study showed that, when possible, gorillas mixed their intake from fruits and leaves to obtain a diet in which protein contributed approximately 19 per cent of available energy intake, which several lines of evidence suggest is close to the target macronutrient balance [138]. In periods when fruit was scarce and the bulk of the diet was contributed by high-protein leaves, the gorillas ingested a diet of 31 per cent protein. Geometric analysis showed that on the high-protein diet the gorillas ingested considerably more protein, but the same amount of non-protein energy as on the low-protein diet, demonstrating that these primates have a different rule of compromise from spider monkeys and humans. While the regulatory responses of Peruvian spider monkeys and mountain gorillas have not as yet been linked to specific conservation objectives, they demonstrate clearly that the consequences of any shift in the macronutrient composition of available foods will be very different for the two species.
A third example concerns a situation in which the rule of compromise remains unknown, but geometric modelling has been used in an attempt to solve an important problem in the conservation of a critically endangered species [140]. The New Zealand Kakapo (Strigops habroptila), of which there are 126 at the time of writing, breed on average once every 2–5 years [141]. Breeding is clearly linked to masting years of fruits of podocarp trees such as rimu (Dacrydium cupressinum), which are the principal food used by females for rearing the young. This strongly suggests that the decision by female kakapo of whether or not to breed is linked to nutrition. Consequently, in 1989, the New Zealand Department of Conservation introduced a supplementary feeding programme with the aim of triggering breeding in years when rimu fruits were not abundant, but this has not been successful [141].

To help understand why the feeding programme has not succeeded in triggering breeding, Raubenheimer and Simpson [140] compared the composition of rimu fruits and ‘muesli’, a supplementary feed that was historically used by the Department of Conservation. The analysis showed that the ratio of macronutrients to calcium was much higher in the supplementary feed than in rimu (figure 10). Without knowing how this imbalance would influence food intake in kakapo, we used nutritional geometry to model three scenarios. If kakapo ate the same amount of the supplemental feed as rimu (e.g. 100 g), it would ingest only 38 per cent the amount of calcium and 580 per cent the amount of macronutrients compared with having eaten the natural food. If it regulated to the same intake of macronutrients, it would ingest only 6.3 per cent the level of calcium when feeding on supplementary food compared with rimu. Alternatively, to achieve the same calcium intake on the two foods a kakapo would need to ingest a massive 15 times the amount of macronutrients when feeding on the supplementary food compared with rimu. Given the strong influence that macronutrients exert on the regulation of food intake, it is most probable that kakapo would not over-ingest macronutrients to any large extent, and would thus suffer a shortage of calcium when feeding on the supplementary food. The importance of calcium for breeding in birds [64] suggests that the high macronutrient:calcium balance of the supplementary feeds might at least partially account for their ineffectiveness in triggering breeding by kakapo. These insights are currently being developed for incorporation into supplementary feeding regimes for kakapo.

7. CONCLUSIONS
The marked similarities in the aims, conceptual structures and methods of NE and CP discussed in §2 of this paper are in no small part due to a common influence that stems from Claude Bernard. As we have attempted to show in §3, the key idea that distilled from Bernard’s interest in the relationships between organisms and their physical environments, the ‘milieu interior’, seeded a lineage of concepts upon which both fields now rest. The base idea, that animals can regulate their functions independent of the physical environment, is central to understanding the ways that individuals persist in the face of environmental change and the limits to their persistence. On the other hand, it is the persistence not just of
individuals, but of populations and lineages that defines NE and CP, and a long-term perspective is needed for this. That perspective, provided by the fields of developmental biology, life-history theory and evolutionary biology (§4), is what sets NE and CP aside from the more narrowly focused physiological sciences. For NE and CP to qualify as scientific fields, however, and not mere labels [142], it is important that they yield concepts, methods and insights that transcend their parent disciplines. In §5, we have attempted to show how one such contribution, nutritional geometry, provides a framework for integrating animal responses to their environments across multiple timescales, and for understanding the functional consequences of these responses. When environmental change is of a magnitude or rate that exceeds the capacity of the adaptive mechanisms, then there is a risk of extinctions. Understanding, predicting and managing this state of mismatch (§6) is an area where we see considerable potential for synergies between NE and CP.

We thank Pedro Texeira for help with formatting. A.H.T. is supported by the Massey University Research Fund, and D.R. is supported by the Massey University Research Fund and the National Research Centre for Growth and Development (New Zealand). S.J.S. has a Laureate Fellowship from the Australian Research Council.

REFERENCES

Phil. Trans. R. Soc. B (2012)