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Temperature and the metabolic theory of ecology

A. CLARKE†

British Antarctic Survey, NERC, High Cross, Madingley Road, Cambridge CB3 0ET, UK

Introduction

The fundamental equation of the Metabolic Theory of Ecology links the metabolic rate of an organism, Q, to its mass, M, and temperature, T, as:

$$Q = b_0 M^b e^{-E/kT}. \quad \text{eqn 1}$$

This equation comprises two components, a power relationship describing the mass dependency (scaling) and a Boltzmann temperature correction. The value of the scaling exponent b is taken to be ~0·75, derived from the physics of distribution networks in animals (West, Brown and Enquist 1997) and plants (West, Brown & Enquist 1999), and b_0 is a normalization constant which is fitted empirically (Brown *et al.* 2004a). Gillooly *et al*. (2001) called the temperature component of the equation the Universal Temperature Dependence of Metabolism (UTD), and its formulation follows from the application of statistical thermodynamics to whole-organism metabolism. Here k is Boltzmann's constant and E the 'mean activation energy of metabolism', its value being estimated empirically from measurements of enzyme kinetics *in vitro* (Gillooly *et al.* 2001).

Recently Clarke (2004) and Clarke & Fraser (2004) have argued that although the UTD is one of several useful statistical descriptions of the relationship between temperature and whole-organism resting metabolism rate, it cannot represent a direct mechanistic dependence of metabolic rate on temperature. This is because of the complex nature of metabolism, and the feedbacks involved in its control. Gillooly *et al*. (2006) have responded robustly, and here we reply to their concerns.

Gillooly *et al*. (2006) make a number of points in their critique, the key ones being:

1. The Boltzmann temperature correction is mechanistic and not statistical (phenomenological), and hence is superior to any other description of the relationship between temperature and metabolic rate.
2. Boltzmann kinetics override any effects of the complexity of cellular physiology.
3. The rate of ATP generation by isolated mitochondria *in vitro* exhibits a temperature sensitivity closely similar to that of whole organisms.
4. The MTE equation can accommodate acclimation or evolutionary adjustment through variation in the normalization constant b_0, and this means that interspecific (between-species) scaling may differ from intraspecific (within-species) scaling.

I suspect that our two views of the relationship between temperature and metabolic rate are closer than the above would imply. It would therefore be sensible to outline where we agree, to distinguish those areas where we do not.

Firstly, it is universally recognized that an acute change of temperature produces a corresponding change in metabolic rate, and it is generally observed that this acute effect is ameliorated by compensatory processes. Secondly, when comparison is made across taxa that have adapted over evolutionary time to live with different body temperatures, there is a strong positive and monotonic relationship between resting metabolic rate and temperature. This relationship is typically close to exponential in shape, and can be linearized by a variety of statistical models.

Where we disagree is in considering the relationship between resting metabolic rate and temperature observed across taxa as simple and mechanistic whereby an increase in temperature is the only factor involved in determining resting metabolic rate (as expressed formally in the MTE equation, and what Clarke (2004) termed the *hard UTD hypothesis*). This strict interpretation of the MTE equation would allow for the effect of temperature on metabolic rate to be ameliorated through adjustments to the mean activation energy, E; Gillooly *et al*. (2006), however, argue that the value of E will remain relatively constant in the range 0·6–0·7 eV.

This difference of viewpoint does not undermine any exploration of the consequences of metabolic scaling for ecology or diversity (e.g. Allen, Brown & Gillooly 2002; Savage *et al*. 2004a; Gillooly *et al*. 2005). Indeed there is a long history of applying allometric relationships to ecology (Peters 1983), the usefulness of which depends essentially on the validity of the ancillary assumptions. However, if the underpinning

†Author to whom correspondence should be addressed. E-mail: accl@bas.ac.uk

scaling relationship is statistical rather than mechanistic, we must accept a limitation in our understanding of the circumstances under which this relationship fails to match reality.

Here I reply to the key issues raised by Gillooly *et al.* (2006) in their critique. But first I make some general points to set the context for my response.

Some general points

West & Brown (2004) describe the MTE equation as the zeroth order relationship linking metabolic rate, body mass and temperature. In other words, after correcting for body mass and temperature, all organisms from bacteria to whales, and from unicellular algae to trees, have the same resting metabolic rate. They do not, of course, as has been known ever since physiologists compared the metabolic rates of ectotherms and endotherms (Fig. 1a). Gillooly *et al.* (2001) recognize this quite explicitly, but the MTE equation cannot predict these differences; it can only describe them statistically through an empirical fit of the normalization constant b_0 to data. An important point here, to which I return later, is the taxonomic level at which the normalization constant is fitted. West *et al.* (1997, 1999) present examples broadly at the level of taxonomic kingdom or class, and the comparison of resting metabolic rates in Fig. 1(a) involves the fitting of the normalization constant at the level of class (reptiles and mammals).

As a second example, data on the resting metabolic rate of teleost fish reveal a strong scaling with body mass (Clarke & Johnston 1999). The overall mean scaling relationship has a value of $b = 0{\cdot}79$, the 95% confidence intervals of which exclude (albeit only just) the theoretical value of 0·75 predicted by West *et al.* (1997). When the fish resting metabolism data are broken down by order it is found that the slope of the relationship is always statistically indistinguishable from the mean value calculated for all fish (General Linear Model, GLM: $P > 0{\cdot}05$) whereas the elevation characteristics of each order differs significantly (GLM, $P < 0{\cdot}05$). This GLM analysis is thus fitting the normalization constant at the level of taxonomic order, describing significant heterogeneity within a taxonomic class (Fig. 1b).

The important point here is whether an ecologist or physiologist is interested in the underlying relationship or the variance. The MTE provides a robust description of an important central tendency in organismal physiology, and such descriptions are of enormous theoretical and practical importance. They allow us to model fundamental aspects of organisms using relatively few variables and parameters and hence to make broad ecological generalizations. The MTE cannot explain why a given species does a particular thing, but this is not its aim. What it does do is provide a powerful description of an important central tendency in biology, against which we can compare the variable real world

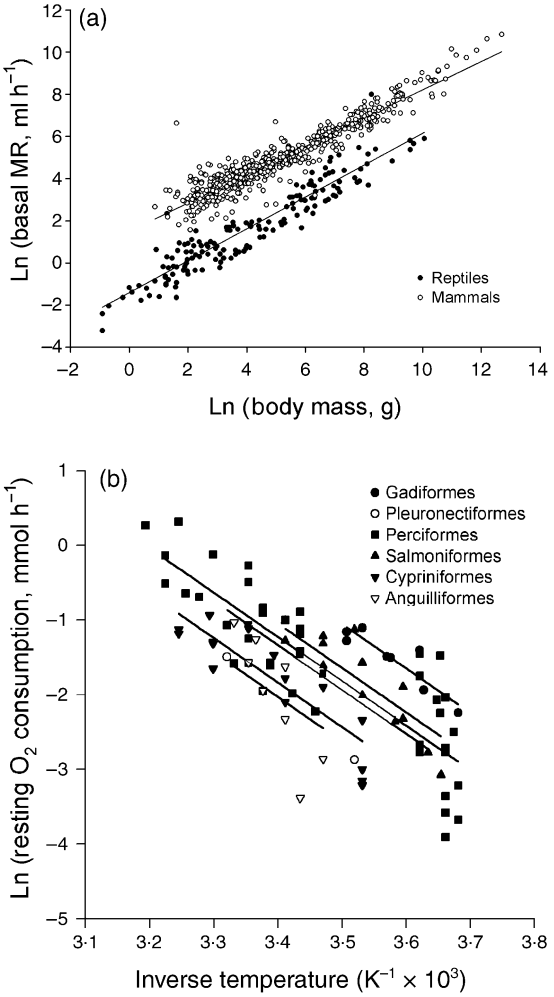

Fig. 1. Scaling of resting metabolic rate in vertebrates. MR = metabolic rate. Data plotted in original units. (a) Reptiles and mammals, scaling of resting metabolic rate with body mass (data from White & Seymour 2003). Both variables log-transformed, with no correction for temperature. All data sets contain only one data point per species, assigned to a median body mass and temperature. Individual regression lines fitted with a General Linear Model (GLM). The GLM is equivalent to fitting the normalization constant at the taxonomic level of class, and indicates statistically significant heterogeneity in slopes ($P < 0{\cdot}001$) and in elevation ($P < 0{\cdot}001$) for a fitted common slope. (b) Teleost fish, scaling of resting metabolic rate with temperature. Here the GLM is equivalent to fitting the normalization constant at the taxonomic level of order (data from Clarke & Johnston 1999). Data are resting metabolic rate calculated for a fish of standard wet mass 50 g, using a scaling coefficient $b = 0{\cdot}789$. The data are plotted in Arrhenius form. The GLM indicates no heterogeneity in slopes ($P > 0{\cdot}05$; that is all orders exhibit similar temperature sensitivity) but highly significant heterogeneity in elevation ($P < 0{\cdot}001$).

(West & Brown 2004). As Harte (2004) has argued cogently, the MTE provides a valuable null theory, but one where much of the interesting biology lies in the deviations from the model. The MTE has thus provided a valuable pointer towards interesting areas of study.

To provide a specific context for this point, consider the data for resting metabolic rate in reptiles and mammals (Fig. 1a). To physiologists the 10–12-fold difference in

mean resting metabolic rate between a typical reptile and mammal is important, reflecting predominantly the energetic cost of an endotherm metabolism (for which the underlying physiology is now well understood: Else & Hulbert 1987; Else, Turner & Hulbert 2004). Also of interest is the heterogeneity in the scaling exponent between different vertebrate classes: in mammals and birds overall $b \sim 0{\cdot}67$ and is statistically quite distinct from the prediction of the MTE which is $b \sim 0{\cdot}75$ (Dodds, Rothman & Weitz 2001; White & Seymour 2003, 2004; White, Phillips & Seymour 2006). At the level of class (all mammals or all birds) this is a robust result which cannot be explained away on the basis of vagaries of taxonomic sampling (as has been argued by West & Brown 2004). Savage *et al*. (2004b) argued that $b \sim 0{\cdot}67$ was the result of an uneven distribution of mass values; they pooled data into 52 mass bins and proposed a value of b close to the MTE prediction of $b \sim 0{\cdot}75$. Two major sources of variance in any overall relationship between resting metabolic rate and mass in mammals are the heterogeneity in scaling relationships with taxonomic order (Kozlowski & Konarzewski 2005) and variation in body temperature (despite the narrow range of body temperatures in mammals: White & Seymour 2003; White *et al*. 2006). These sources of error, however, affect all such broad compilations; they apply equally to those groups where the fitted exponent matches the MTE prediction as to those where it does not.

The major mass-related error in measures of resting metabolic rate in mammals and birds probably comes from the influence of circadian rhythms (Aschoff 1982), which makes it more likely with decreasing size that any measured metabolic rate will not be representative, and hence that the fitted relationship overestimates the true slope. Recent debates have also considered the separate issue of measurement error, and Farrell-Gray & Gotelli (2005) have shown from a careful meta-analysis that errors in body mass estimates may be more pervasive than previously thought: whilst the body mass of any individual may be measured precisely, the error comes from selection of an inappropriate value to represent a given species. The critical point is thus whether the data for mammals and birds are an interesting deviation from the central tendency described by the MTE equation, or a fundamental challenge to the theory itself. It is intriguing that the two groups whose scaling most differs from the scaling relationship predicted by the MTE are both endotherms; perhaps in birds and mammals considerations of heat flow override the scaling dictated by fractal-like supply networks.

A recent study of metabolic rate in insects suggests that here also resting metabolic rate exhibits $b \sim 0{\cdot}67$, perhaps reflecting a very different system for oxygen delivery to the tissues (Niven & Scharlemann 2005), although an earlier study of a more comprehensive data set had indicated a steeper slope for arthropods (Addo-Bediako, Chown & Gaston 2002). More recently the applicability of a universal $b \sim 0{\cdot}75$ has been questioned for terrestrial plants (Li, Han & Wu 2005; Reich *et al*. 2006), a comprehensive analysis by Glazier (2005) has revealed considerable heterogeneity in the value of b across a wide range of animal groups, and Makarieva, Gorshkov & Li (2003, 2005) have examined the scaling of metabolic rate from the perspective of a minimum cost for maintaining living tissue. The question of the scaling of metabolic rate is far from resolved.

The sequence of points made by Gillooly *et al*. (2006) centre on two key issues, namely the relevance of a simple Boltzmann correction to complex physiology and the difference between within-species and between-species scaling relationships. Rather than reply to their critique point-by-point, I will discuss these two issues, identifying areas of agreement, disagreement and misinterpretation.

Statistical thermodynamics and complex physiology

All discussions of the thermal physiology of organisms acknowledge their debt to the Stefan–Boltzmann equation and the Arrhenius concept of activation energy. Despite its intuitive appeal, however, there are many reasons why classical statistical thermodynamics can be extrapolated to whole-organism physiology only with great care.

Although originally developed for bimolecular reactions in the gas phase under ideal conditions, classical statistical thermodynamics provides a powerful explanation for the reaction rate of simple processes in dilute solutions under equilibrium conditions. The key problem, long recognized by physiologists, is that organisms are complex, non-equilibrium systems and the cell contents are far from ideal dilute solutions. Most important, however, is that statistical thermodynamics is based on the assumption that all the entities under consideration are identical, and that the only change in the system is its temperature. Neither assumption is valid for organismal physiology. In particular, organisms that have evolved to live at different temperatures have enzymes with different kinetic behaviour, mitochondria with different composition, structure and kinetics, and a different intracellular milieu. Clearly an organism is very different from the simple system to which classical statistical thermodynamics applies.

Nevertheless it is well established empirically that resting metabolic rate increases monotonically with temperature. Gillooly *et al*. (2001, 2006) argue that a strong statistical fit to a simple Arrhenius model indicates that predictions of the MTE are well supported. Clarke & Johnston (1999) showed clearly that in a carefully selected data set for teleost fish the relationship between resting metabolic rate and temperature was described equally parsimoniously by any one of three statistical models (Arrhenius, exponential, double-logarithmic). As commented by Gillooly *et al*. (2006) we did suggest that in the absence of any other evidence we would use the Arrhenius model; however, this was a choice of statistical model, not of underlying

mechanism. The difference in viewpoint here is that Gillooly *et al*. (2001) plot their data in Arrhenius form on the basis of the MTE model and are happy with the fit to data (though the variation in fitted slope for various groups is ~15%). In contrast Clarke & Johnston (1999) set out with no *a priori* assumptions concerning underlying mechanisms, and simply compared the fit of different statistical models.

Entropy and the role of water

A critical difference between the views of Gillooly *et al*. (2001) and Clarke (2004) concerns the extent to which the relationship between temperature and metabolic rate is influenced by the complexities of cellular physiology. Clarke (2004) emphasized the importance of feedbacks in metabolic control and of entropy in enzyme kinetics, but Gillooly *et al*. (2006) dismiss these effects as trivial. This misunderstands the role of entropic effects in the complex sequence of events involved in enzyme catalysis, events in which water plays an integral role. To see why entropy is important, it is necessary to consider the thermodynamics of enzyme catalysis.

The basic theory of reaction kinetics was developed for simple dilute aqueous systems involving small molecules, where processes are typically dominated by enthalpic changes. The enzyme-mediated processes that characterize physiology are far more complex. They take place either in a complex gel-like cellular environment, or on a membrane. In particular, water is not only a solvent but is also a reactant or product in all the major classes of reaction (condensation, hydrolysis, hydrogenation, dehydrogenation). The most important role for water, however, comes through the weak-bond interactions with protein molecules. Weak bonds such as hydrogen bonds have low vibrational frequency, and this gives them appreciable entropy. Because the process of ligand binding and release involves conformational changes, it necessarily results in the formation or breakage of many hydrogen bonds. In consequence entropy changes dominate many of the interactions between proteins and ligands. These ligand binding and release processes are typically the rate-limiting steps in enzyme catalysis, and the overall kinetics require sophisticated modelling using transition-state theory (see Fersht 1999).

Whilst this emphasizes the important contribution of entropy to enzyme catalysis, determining the individual contributions from enthalpy and entropy is made difficult by enthalpy–entropy compensation in water itself. Enthalpy–entropy compensation has long been recognized as an important feature of the thermodynamics of enzyme kinetics and in evolutionary adaptation, although the concept has been criticized (most notably by Cornish-Bowden 2002; but also by Sharp 2001 and Villà *et al*. 2000). Cornish-Bowden (2002) emphasized important statistical difficulties in the traditional protocol for detecting enthalpy–entropy compensation, and argued that this cast doubt on the existence of such compensation. The statistical point is entirely valid, but enthalpy–entropy compensation is now recognized as a real phenomenon and its origins in the thermodynamics of weak bonds in water is well understood (Dunitz 1995; Fersht 1999). Current knowledge of the thermodynamics of enzyme catalysis thus identifies clearly the importance of entropy, and highlights the role of weak bonds; there is more than enthalpy (temperature) to the determination of reaction rate in physiology.

From cells to organisms: feedbacks, supply and demand

Gillooly *et al*. (2006) compare the temperature sensitivity of mitochondrial ATP production *in vitro* with that of whole-organism metabolic rate. Whilst mitochondrial ATP production undoubtedly accounts for a considerable fraction of whole-organism oxygen consumption but physiologists have long recognized that mitochondria held *in vitro* are in a very different environment from that *in vivo*. Most importantly the experiments are undertaken in fully oxygenated media, so that electron acceptors are not limiting, whereas *in vivo* oxygen tensions are very much lower (Egginton *et al*. 2002).

Perhaps most critical for the argument developed by Gillooly *et al*. (2006) is that elsewhere they have argued that isolated cells and organelles held *in vitro* are freed from constraints of nutrient supply and thus deviate from the predictions of the MTE equation, though in ways that verify their model (West & Brown 2004). This is not to say that experiments *in vitro* cannot provide fundamental insights into physiology, only that extrapolation to *in vivo* is not at all straightforward because of the complications of resource supply, feedbacks and higher level metabolic controls. Indeed the strong dependence of mitochondrial ATP production on temperature revealed by *in vitro* experiments may be a fundamental constraint on whole-organism energetics, ecology and life history (Clarke 2003). That this dependence is not a direct mechanistic relationship to temperature is indicated by the extent to which it is affected by seasonal acclimatization (Guderley & St Pierre 1996), and also that the temperature sensitivity of ATP generation and mitochondrial proton leak is quite different (Hardewig, Peck & Pörtner 1999).

Cells do not, however, make ATP regardless. ATP synthesis is tightly regulated with the key control mechanisms being well known and long established. Particularly important are energy charge (a measure of the ratio of ATP concentration to that of less phosphorylated forms) and feedback control by intermediary compounds in the citric acid cycle: as ATP stores are replenished ATP synthesis slows. The synthesis of ATP, and hence the requirement for oxygen as electron acceptor, is driven by demand for ATP (Fig. 2a). In direct contrast, the MTE equation links metabolic rate mechanistically and directly to temperature; for an organism whose mass stays constant there are no other

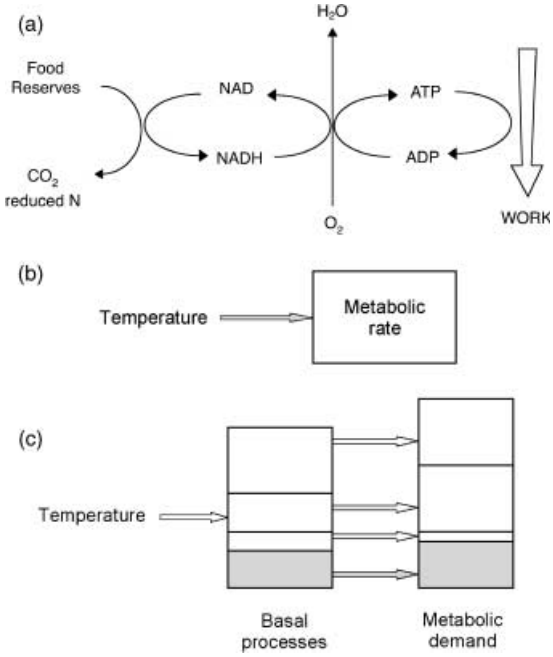

Fig. 2. Direct and indirect effects of temperature on metabolic rate. (a) A conceptual diagram showing how the rate of production of ATP, and hence demand for oxygen, is driven by the requirement for physiological work. If demand slows, then feedback controls slow the rate of ATP generation. This is thus a demand-driven process. (b) The Metabolic Theory of Ecology, whereby the temperature of an organism dictates its metabolic rate directly. This is a supply driven process. (c) The model of Clarke (2004). Here the temperature dictates the level of the suite of processes comprising resting (basal) metabolic rate; and the total demand for oxygen sets the level of basal metabolic rate. This is an indirect effect of temperature on metabolic rate, and is a demand-driven process. The relative sizes of the boxes are arbitrary, and repair processes are shown highlighted in grey.

driving variables in the equation. This is thus a supply-driven mechanism: if temperature increases, ATP generation and hence metabolic rate increase (Fig. 2b).

Gillooly *et al*. (2006) argue that in organisms supply and demand are always in balance. This is indeed true; any viable organism must be able to supply the ATP that circumstances demand. As metabolic demand increases (for example for locomotor activity or post-prandial growth) then cardiovascular supply increases until a mechanical limit is reached. The point made by Clarke (2004) was subtly different, and is summarized in Fig. 2(c). As temperature increases, the rate of many processes (but not necessarily all) making up resting metabolic rate increases. These might include membrane turnover, protein turnover, ion balance, mitochondrial proton leak and hence include changes in the rate of many repair mechanisms which may require trade-offs between competing processes if ATP demand reaches the maximum rate at which it can be supplied. The nature and extent of the impact of temperature on these different processes vary (Hardewig *et al*. 1999; Clarke & Fraser 2004) but the net effect is an increased demand for ATP, which is seen as an increase in whole-organism oxygen demand. The relationship between temperature and metabolic rate is thus indirect, complex and not easily modelled mechanistically. It can, however, be described statistically and the ecological consequences of the observed empirical relationship be explored (Clarke 1987, 1993, 2003).

Evolutionary trade-offs and metabolic cold adaptation

Gillooly *et al*. (2006) equate the evolutionary trade-off hypothesis (Clarke 2004; Clarke & Fraser 2004) with metabolic cold adaptation. We clearly did not express ourselves well, for regarding these two phenomena as equivalent misunderstands both.

The concept of metabolic cold adaptation (MCA) followed early work on the thermal physiology of fish by August Krogh. The specific hypothesis was that organisms which had adapted over evolutionary time to live at low temperatures would have a resting metabolic rate higher than expected from the metabolic rate/temperature relationship established for fish living at warmer temperatures (for more detail see Holeton 1974; Clarke 1980, 1991). This would be equivalent to polar fish having a higher value of the normalization constant b_0 than other fish (or alternatively, that polar fish would lie above the central tendency line expressed by the MTE equation for all fish). Experimental data show clearly that, at least in fish, MCA *sensu* Krogh does not exist (Holeton 1974; Clarke & Johnston 1999). Subsequent to Krogh's seminal work, the concept of MCA was broadened to include the widely reported changes in the nature or amount of enzymes or lipids (Hochachka & Somero 2002), but these intracellular adjustments are best seen as an aspect of adaptation or acclimation to temperature in a wider sense.

The evolutionary trade-off hypothesis is quite different. It argues that the resting metabolic rate of an organism is the result of a trade-off between resting costs and scope for activity, with the precise level being set by lifestyle. It therefore explains why a group of organisms such as fish comprise different groups characterized by different resting metabolic rates (quantified by differences in the value of the normalization constant b_0) (Fig. 1b). The hypothesis was first elaborated in Clarke (1993) but only given the name by Clarke (2004). The conceptual basis is the indirect influence of temperature on cellular processes coupled with evolutionary trade-offs involving relative tissue mass (Clarke & Johnston 1999). It is conceptually identical in its basis to the allometric cascade hypotheses of Darveau *et al*. (2002) and Hochachka *et al*. (2003), who develop this idea in a formal scaling context.

Gillooly *et al*. (2006) criticize this idea as unclear, non-quantitative and difficult to test. The basic idea is clearly laid out in the conceptual model presented (Fig. 3a), and some broad predictions do follow (for example that organisms with more active lifestyles will be characterized by higher resting metabolic rates,

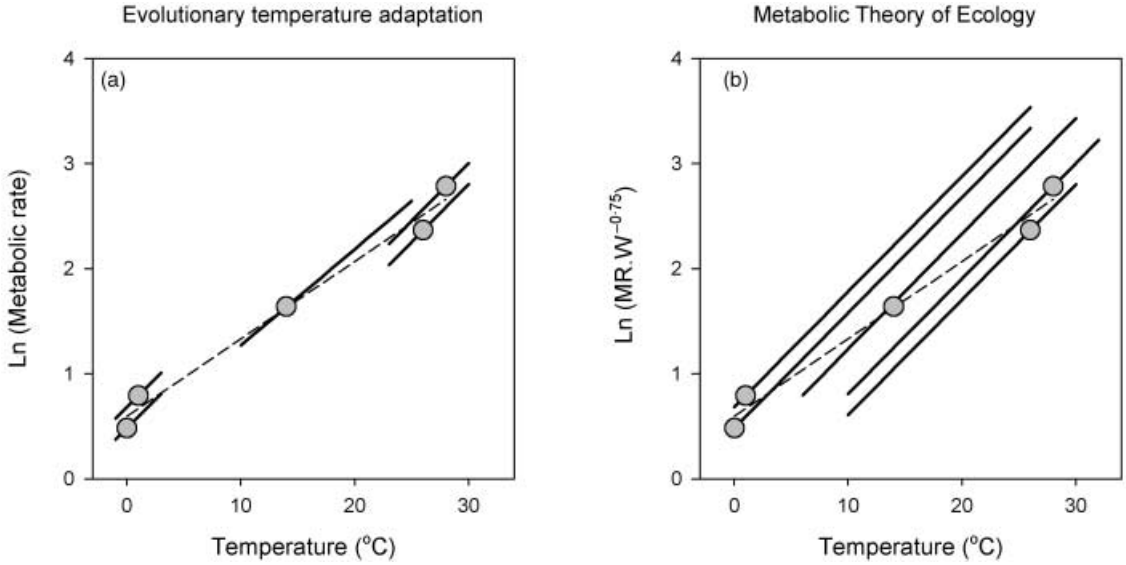

Fig. 3. Conceptual models of the relationship between resting metabolic rate (MR) and temperature in ectotherms. (a) The Evolutionary Trade-off Hypothesis. The plot shows the metabolic rate/temperature relationship for five hypothetical organisms, two living at a cool temperature, one at a moderate temperature and two at a high temperature. The lines represent the acute effect of temperature on each species, assuming an arbitrary but biologically reasonable Q_{10} of 2·5. The circles represent the resting metabolic rate for each species at its normal living temperature. The across-species relationship is different in kind, and here also in slope, from the within-species relationship (note that in this diagram the difference in slopes has been exaggerated for clarity). It is also different in kind, being a statistical population of individual evolutionary optimizations. Redrawn from Clarke & Fraser (2004). (b) The Metabolic Theory of Ecology. The plot shows the within-species relationships for five hypothetical species, as for Fig. 3(a), but with metabolic rate corrected for body mass according to the MTE. These five species have been shown as individual relationships, which require the fitting of the normalization constant, b_0, of the MTE equation to individual species. The across-species relationship is thus different in kind, and here also different in slope, being a statistical population of individual evolutionary optimizations. Note that here also the difference in slopes has been exaggerated for clarity.

such as observed in arthropods: Reinhold 1999; Addo-Bediako *et al*. 2002), but the model is primarily explanatory. It cannot predict the resting metabolic rate of a particular species, any more than the MTE can. A crucial difference is that whereas the MTE predicts a grand central tendency for all organisms, the evolutionary trade-off hypothesis is concerned with explaining both the overall relationship between resting metabolic rate and temperature, and the cause of variation about this. It cannot make quantitative predictions because of the inherent complexity of physiology and the nature of the trade-offs involved, but it does explain how this complexity generates physiological diversity. It is thus quite different in aim from the MTE, which subsumes this diversity within a single relationship.

From species to general models

A critical aspect of the application of the MTE equation is the taxonomic level at which the normalization constant, b_0, is fitted to empirical data. West *et al*. (1997, 1999) fitted the equation to the broadest possible suite of taxa, from unicellular algae to trees, and from prokaryotes to whales, producing a grand central scaling relationship for all living things. The authors acknowledge explicitly that the fit contains variance from a variety of sources some systematic (such as temperature: Gillooly *et al*. 2001), others stochastic. Whilst this overall MTE relationship captures a broad pattern for all of life, it simultaneously obscures differences that many ecologists and physiologists regard as important, for example the large differences in resting metabolic rate between endotherms and ectotherms. Fitting the normalization constant at the level of class (Fig. 1a) captures this difference, but at the expense of generality both in terms of b_0 and the scaling exponent. Fitting at the level of order (Fig. 1b) exposes further phylogenetically related heterogeneity.

If the MTE equation is fit to individual species to allow for evolutionary adaptation (as proposed by Savage *et al*. 2004b and Gillooly *et al*. 2006), then each species represents the outcome of a quasi-independent evolutionary process. All generality is thereby lost, and the MTE becomes effectively identical to the evolutionary trade-off hypothesis (Fig. 3b). The evolutionary adjustment is of course only quasi-independent because of phylogenetic constraints. Much debate surrounding the applicability of the MTE to ecology or physiology thus concerns the taxonomic level at which it is applied. At the highest level the MTE equation generalizes broadly but misses important evolutionary detail; at lower levels generality is lost and evolutionary heterogeneity in both the normalization constant and the scaling exponent is exposed.

Clarke (2004) argued that an implicit assumption of the MTE was that interspecific and intraspecific scaling should be identical, because the same physical principles underpin both. Savage *et al*. (2004b) and

Gillooly *et al*. (2006) both argue that evolutionary adjustment of metabolic rate takes place through variation in the normalization constant b_0, which is precisely the mechanism that many authors (e.g. Darveau *et al*. 2002; Clarke 2004) have argued removes the generality of the MTE. Using a wider range of data than Clarke & Johnston (1999), employing a different mass correction protocol and a different temperature sensitivity, Gillooly *et al*. (2006) make a convincing case that, at least in teleost fish, within-species and between-species scaling of resting metabolic rate with temperature are statistically identical.

Concluding remarks: the challenge of the Metabolic Theory of Ecology

Like all good theories, the Metabolic Theory of Ecology challenges us to look again at how we view the world. It also produces unexpected results, such as the scaling relationship based on organisms with highly structured vascular systems appearing to apply also to organisms with open circulations, unicells, mitochondria and even isolated reaction centres. It is in these areas that the theory will be challenged most strongly (Makarieva *et al*. 2005).

The theory also sets a challenge to the more complex views of thermal physiology advanced by Darveau *et al*. (2002), Hochachka *et al*. (2003) and Clarke (2004). In particular it is not at all clear why the slope of relationship between resting metabolic rate and temperature in organisms is so similar to that exhibited by simple systems. Gillooly *et al*. (2001, 2006) interpret this as indicating an overwhelming and direct control of metabolic rate by temperature. Physiologists concerned with the detail of how organisms actually work would argue that the complex interactions involved mean that the relationship is more subtle and complex, involving evolutionary trade-offs at all levels (Clarke 1993, 2004; Darveau *et al*. 2002). This complexity would necessarily mean that the relationship between metabolic rate and temperature can be only a statistical description of a collection of separate evolutionary optimizations (albeit with a strong phylogenetic content: Clarke 2004).

The critique that the mechanistic basis of the MTE is unrealistically simplistic when compared with what we know of organismal physiology is not confined to Clarke (2004). Marquet, Labra & Maurer (2004) argue that a Boltzmann temperature correction can be regarded only as an approximation of a much more complicated functional relationship between metabolism and temperature; Cyr & Walker (2004) argue that the complex way in which organisms utilize energy and metabolites means that, as yet, there are no short cuts to simple models that are valid; and Cottingham & Zens (2004) argue that the data available do not yet provide clear links to physical and chemical first principles that would support the formulation of the MTE equation. Common to all these critiques is that the relationship between metabolism (indeed all physiology) and temperature is complex, and hence at present any overall description of this relationship must be statistical (phenomenological).

Looking in the opposite direction, the challenge to physiologists from the MTE is to explain why the relationship between metabolic rate and temperature is what it is. Metabolism comprises a complex suite of processes, some catalysed by enzymes, some dominated by physical processes such as diffusion, and others involving quantum behaviour which is temperature invariant, all of which take place in a complex, highly structured, gel-like environment. It would seem that nothing could be further from the simple dilute systems of statistical thermodynamics and yet the relationship between whole-organism metabolic rate and temperature is a deceptively simple one, which almost demands a simple explanation in terms of a single governing process. Perhaps the answer lies in the central importance of water to enzyme kinetics and the temperature dependence of weak bonds, possibly combined with diffusional constraints, rather than simple kinetics. As Brown *et al*. (2004a,b) and Gillooly *et al*. (2006) acknowledge, the complex links between temperature and whole-organism metabolic rate are one of the areas of physiology where further detail is needed. I could not agree more.

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