INVITED PERSPECTIVES IN PHYSIOLOGICAL AND BIOCHEMICAL ZOOLOGY

Thermodynamic Effects on Organismal Performance: Is Hotter Better?

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ABSTRACT

Despite decades of research on the evolution of thermal physiology, at least one fundamental issue remains unresolved: whether the maximal performance of a genotype depends on its optimal temperature. One school argues that warm-adapted genotypes will outperform cold-adapted genotypes because high temperatures inevitably accelerate chemical reactions. Yet another school holds that biochemical adaptation can compensate for thermodynamic effects on performance. Here, we briefly discuss this theoretical debate and then summarize empirical studies that address whether hotter is better. In general, comparative and experimental studies support the view that hotter is better. Furthermore, recent modeling has shown that thermodynamic constraints impose unique selective pressures on thermal sensitivity. Nevertheless, the thermodynamic effect on maximal performance varies greatly among traits and taxa, suggesting the need to develop a more sophisticated view of thermodynamic constraints.

Introduction

The behavior, physiology, and fitness of organisms depend strongly on body temperature. This thermal sensitivity has been commonly depicted as a tolerance curve (Levins 1968) or a performance curve (Huey and Stevenson 1979). These curves share several important properties, including a unimodal shape, a negative skew, and a finite breadth. Physiologists generally describe these curves in terms of three key parameters: (1) the optimal temperature (or thermal optimum), which defines the temperature that maximizes performance; (2) the thermal breadth (or performance breadth), which defines the range of temperatures that permit some level of performance; and (3) the maximal performance, which defines the level of performance at the optimal temperature (see Fig. 1). By comparing these parameters among populations or species, physiologists have answered some fundamental questions about the evolution of performance curves (Huey and Kingsolver 1989). Does thermal sensitivity evolve rapidly or slowly (Bogert 1949; Huey et al. 2003)? Does selection for enhanced performance at one temperature reduce performance at other temperatures (Hertz et al. 1983; Bennett et al. 1990)? And does a decrease in thermal breadth yield greater performance at the optimal temperature (Huey and Hertz 1984; Gilchrist 1995)? But one question has received much less attention, namely, does selection for a higher optimal temperature cause a correlated increase in maximal performance? In other words, is hotter better? The theoretical basis and empirical resolution of this question constitute the subjects of this perspective.

The answer to this question depends on the relative powers of thermodynamic constraint versus biochemical adaptation (Clarke 2003; Frazier et al. 2006). Proponents of the thermodynamic constraint hypothesis hold that low body temperatures inevitably depress rates of biochemical reactions, such that organisms adapted to lower temperatures (i.e., having lower thermal optima) will perform relatively poorly at their thermal optima (Fig. 2*A*). Proponents of the biochemical adaptation hypothesis counter that changes in molecular and cellular structures can compensate for any thermodynamic advantages of high temperatures. If so, species adapted to low temperatures will perform at the same levels as species adapted to high temperatures (Fig. 2*B*).

These two hypotheses polarize the debate. Of course, no one denies that thermodynamics ultimately constrain performance. At the same time, no one denies that biochemical adaptation buffers performance. Thus, the real issue is whether thermodynamics set narrow or broad boundaries on evolutionary patterns (Clarke 2006). If thermodynamic constraints dominate, biochemical adaptation can compensate for only small shifts in thermal sensitivity. But if thermodynamic constraints are less dominant, biochemical adaptation can compensate for much broader shifts in thermal sensitivity.

Here, we provide a conceptual and empirical perspective on thermodynamic constraints during adaptation. We begin by tracing the development of the debate from its origin and sum-

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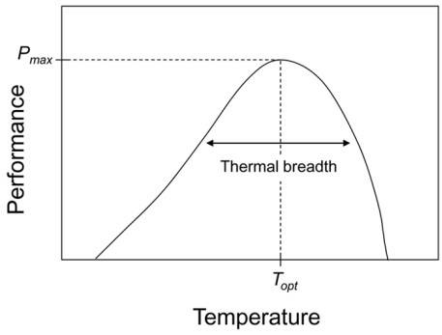

Figure 1. Hypothetical curve depicting the thermal sensitivity of performance. The optimal temperature (T_{opt}), thermal breadth, and maximal performance (P_{max}) are labeled. Adapted from Huey and Stevenson (1979) with permission from Oxford University Press.

marizing the controversy surrounding a recent theoretical model that predicts hotter is better. Then, we review empirical evidence from comparative and experimental studies of performance curves. These studies represent diverse approaches to analyzing phenotypic variation within and among populations or species. We hope that such a broad survey will provide a general and robust answer to whether hotter is indeed better. Finally, we discuss the implications of this thermodynamic constraint for the coadaptation of thermoregulatory behavior and thermal physiology.

Origins of the Debate

The notion that hotter is better traces to the basic laws of thermodynamics, which describe the exponential effect of temperature on the mean kinetic energy of molecules and on rates of biochemical reactions. To our knowledge, Barcroft (1934) was the first to conjecture that physical laws constrain thermal adaptation, and he referred to this hypothetical constraint as the tyranny of thermodynamics. Many decades later, Hochachka and Somero (1973, p. 183) provided a mechanistic basis for thermodynamic constraints on physiological performance in their seminal book, *Strategies of Biochemical Adaptation*. They noted that a 10°C increase in body temperature (within the biological range) results in an ~3% increase in the mean kinetic energy of molecules, which in turn increases the rate of collision (Mortimer 2000). All else being equal, higher temperatures should yield faster biochemical reactions, which could improve performance at the organismal level.

In the 1970s, empirical evidence of thermodynamic constraints, along with some evolutionary implications, began to emerge. By compiling published data on growth rates of marine phytoplankton, Eppley (1972) discovered that maximal growth rate increased by approximately sixfold over a 30°C range of temperatures. His analysis caught the attention of many evolutionary physiologists (including some working in terrestrial systems), and his article appropriately became a citation classic. One year later, Hamilton (1973) invoked thermodynamics to explain why birds, mammals, and other taxa independently evolved the endothermic regulation of high body temperatures. Hamilton (1973, p. 18) argued that selection for higher "metabolic and growth rates" resulted in a correlated rise in body temperature, up to an inviolate limit. His concept of maxithermy clearly assumes a thermodynamic advantage of high body temperature, as suggested by Eppley's comparative analysis. Heinrich (1977, p. 632) soon countered the notion of thermodynamic constraint, stating that Hamilton "appears to overemphasize Q_{10} while ignoring biochemical adaptation. … The hypothesis does not explain why the animal's biochemical machinery has not evolved to do the same job at lower temperature." Thus, Heinrich favored a hypothesis based on evolutionary adaptation rather than one based on physical constraint. He proposed that the thermal set points of mammals and birds evolved to promote heat loss rather than enhance performance. The debate between Hamilton and Heinrich reflected a long-standing tension between researchers who sought to extrapolate from simple biochemical systems to whole-organismal processes and those who saw serious problems with doing so (Prosser 1973; Hoar 1975; Clarke 2004).

Over the next few decades, indirect evidence of thermodynamic constraints accumulated gradually (reviewed by Huey and Kingsolver 1989). For example, Bennett (1987) showed that animals could achieve greater locomotor performance at higher body temperatures, regardless of their preferred body temperatures; in light of this observation, he coined the phrase "warmer is better." Other researchers soon reinforced Bennett's intraspecific comparisons with interspecific analyses in a phylogenetic context. These analyses revealed that species of lizards with higher body temperatures tended to run faster or longer (Garland 1994; Van Damme and Vanhooydonck 2001). Nev-

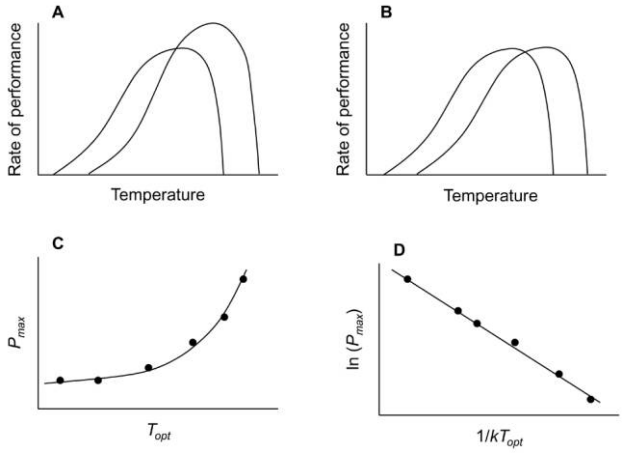

Figure 2. *A*, *B*, Performance curves of warm- and cold-adapted species that accord with either the thermodynamic constraint hypothesis (*A*) or the biochemical adaptation hypothesis (*B*). *C*, According to the model of Savage et al. (2004), we should expect an exponential relationship between the optimal temperature of performance (T_{opt}) and the maximal performance (P_{max}). *D*, On an Arrhenius scale, the thermodynamic effect on maximal performance would appear as a linear relationship between the inverse of the optimal temperature and the natural logarithm of performance.

ertheless, these patterns do not clearly distinguish between thermodynamic constraint and biochemical adaptation because the studies were based on field body temperatures, which do not always indicate optimal temperatures for performance (see Huey et al. 1989). In fact, warmer lizards could have performed better merely because their body temperature was closer to the optimal temperature for performance (i.e., an acute thermal sensitivity of performance), even if species shared the same performance curve. Therefore, a critical distinction exists between Bennett's version of warmer is better and the thermodynamic constraint hypothesis (which unfortunately goes by a similar catch phrase, hotter is better). In light of this distinction, efforts to model or confirm thermodynamic constraints on the evolution of performance must focus on the relationship between the optimal temperature and the maximal performance (see Fig. 2).

A Formal Model of Thermodynamic Constraints

The old debate resurfaced with new vigor following the development of the metabolic theory of ecology (Brown et al. 2004), which mathematically embodied the thermodynamic constraint hypothesis. Building on the foundation of that theory (Gillooly et al. 2001, 2002), Savage et al. (2004) modeled the rate of population growth as a function of body size and body temperature. For a population with stable distributions of ages and sizes, they found that the thermal sensitivity of population growth reduces to an elegantly simple equation:

$$r \approx aM^{-1/4}e^{-E/kT,} \quad (1)$$

where r is the intrinsic rate of population growth, a is a normalization constant (specific to the taxon and the environment), M is body mass, E is the mean activation energy of rate-limiting reactions, k is the Boltzmann's constant, and T is the absolute temperature of the organism. This equation enables one to predict the rate of population growth—a direct estimate of the fitness of a genotype in a growing population—from an organism's mass and temperature.

The thermal sensitivity of r was represented by $e^{-E/kT}$, which physicists refer to as the Boltzmann factor (Haynie 2001). This term dictates that r increases exponentially with increasing temperature (Fig. 2*C*) or that the natural logarithm of r decreases in direct proportion to the inverse of absolute temperature (Fig. 2*D*). Consequently, the thermal sensitivity of r represents a thermodynamic constraint on all organisms: genetic variation in performance occurs only through shifts in body mass (M) or the normalization constant (a). Importantly, the model predicts the quantitative relationship between evolutionary changes in the optimal temperature and the maximal performance; specifically, the slope of this relationship between $1/kT_{\text{opt}}$ and $\ln r_{\text{max}}$ should equal $-E$, or -0.6 eV, according to empirical studies of enzymes. Thus, the model not only predicts that hotter is better but also predicts by how much.

To test their model, Savage et al. (2004) compiled data from laboratory studies of the population growth rates of unicellular and multicellular eukaryotes. Slopes of relationships between $1/kT$ and $\ln r$ were negative and varied from -0.35 to -0.84 eV, bounding the predicted slope. Nevertheless, certain features of their analysis undermine its ability to test the thermodynamic constraint hypothesis. To estimate the thermodynamic effect, Savage et al. (2004) analyzed population growth rates at several temperatures for each species, rather than analyzing only the maximal rate for each species (as shown in Fig. 2). By including multiple rates per species, their analysis confounded acute sensitivities to temperature and thermodynamic constraints on evolution (if the latter exist). Even if one datum were chosen per species, we still must assume that the body temperatures used in the analysis correlated positively with the optimal temperatures for population growth. Note that Savage et al. (2004) did not intend to address evolutionary processes, and thus the shortcomings of their analysis represent our effort to extend their work beyond its original scope.

The model of Savage et al. (2004), along with other components of the metabolic theory, sparked strong reactions from physiologists. Clarke (2004, 2006) stressed the dangers of using insights about simple biochemical reactions to generate universal principles for complex organisms. In Clarke's view, the success of the metabolic theory reflects a good statistical fit between the Arrhenius model and empirical data rather than support for a particular mechanism. Indeed, Hochachka (1991) hypothesized that natural selection, rather than thermodynamics, better explains the relatively narrow range of thermal sensitivities observed among ectotherms. Others have theoretically demonstrated that thermal sensitivities of organismal performance cannot be deduced from the underlying reactions (Chaui-Berlinck et al. 2004). Defenses (Gillooly et al. 2006) and criticisms (Terblanche et al. 2007) of the metabolic theory have continued unabated. Thus, the founders of this theory rekindled a crucial debate about the relative powers of thermodynamics and adaptation. Here, we provide an empirical synthesis to facilitate further discussion between the sides. Because the issues that fuel this debate are extremely complex, we do not expect our synthesis to catalyze a simple or imminent consensus. But we do hope a heated debate will continue; in matters of scientific inquiry, hotter debates are often better.

Evidence for the Thermodynamic Constraint Hypothesis

Intra- and Interspecific Comparisons

A powerful means of testing evolutionary hypotheses involves comparisons of populations or species (Martins and Garland 1991). With regard to the thermodynamic constraint hypothesis, one would compare genotypes with different thermal sensitivities and determine whether performance increases with the optimal temperature of the genotype (Huey and Kingsolver 1989). Frazier et al. (2006) were the first to adopt this approach to specifically test the thermodynamic constraint hypothesis. They compiled thermal sensitivities of population growth rate (r) for 65 species of insects. Overall, they found that populations of warm-adapted species grew faster than populations of cold-adapted species, lending qualitative support to the notion of a

thermodynamic constraint. But the relationship between $1/kT_{opt}$ and ln r was steeper than that predicted by the model of Savage et al. (2004). Thus, hotter was even better than anticipated. Because Frazier et al. (2006) used phylogenetic comparative methods and evaluated alternative hypotheses, their conclusion seems fairly robust. A subsequent analysis of the growth rates of viral populations uncovered a similar pattern: hotter is even better than expected from the current model (Knies et al. 2009). These studies strongly supported the thermodynamic constraint hypothesis, but the patterns they generated pose some fundamental questions. Do thermodynamics influence the population growth rates of other taxa in a similar manner? If so, why should thermodynamics affect population growth so strongly? And does a similar thermodynamic effect constrain behavioral and physiological performances?

To address these questions, we conducted a meta-analysis of published and unpublished data (Table 1). Each study comprised measures of performance at five or more temperatures for at least four taxa (species or populations). Studies were excluded if the authors reported performance only on a relative scale or if they did not cover a sufficient range of temperatures to resolve the optimal temperature; as a rule, we excluded cases in which the maximal performance and the performance at thermal extremes differed by less than 5%. For some cases where insufficient data were reported, we were able to obtain the necessary data from the authors (Carrière and Boivin 1997; Wilson 2001; Palaima 2002). Our final set included 21 studies, with samples ranging from 4 to 143 taxa per study.

For each performance curve, we determined the optimal temperature and the maximal performance. If possible, we obtained these data from tables or functions reported by the authors. Otherwise, we digitized the performance curves and extracted values of temperature and performance using Data Thief III (http://www.datathief.org). Once these data were obtained, we used van Berkum's (1986) minimum convex polygon method to identify optimal temperatures and maximal performances. We then explored the relationship between these parameters for each study. Maximal performances were transformed to natural logarithms to meet the assumption of linearity. When appropriate, we adjusted maximal performance for body size (length or mass) to yield a semipartial correlation. Because we wanted to compare the slopes of these relationships to a theoretical prediction (Savage et al. 2004), we regressed the natural logarithm of maximal performance onto $1/kT_{opt}$. The correlation coefficient of each relationship was used in our meta-analysis. Each correlation coefficient was converted to an unbounded measure of effect size using Fisher's z transformation (see Gurevitch and Hedges 1993). An unstructured model was used to estimate the mean effect size. Unbiased 95% confidence intervals were estimated by bootstrapping. All meta-analytical procedures were performed with MetaWin 2.1 (Rosenberg et al. 1997).

Table 1: Summary of comparative studies included in our meta-analysis

Taxa	Performance	Measurements	Correlation Coefficient	No. Taxa	Source
Frogs	Locomotion[a]	Swimming speed	.10	5[b]	Navas 1996*a*, 1996*b*
Marsh frogs	Locomotion	Jumping speed	−.96	5	Wilson 2001
Lizards	Locomotion[a]	Sprinting speed	−.42	10[b]	Bauwens et al. 1995
Lizards	Locomotion[a]	Sprinting speed	−.21	7	van Berkum 1986
Mites	Locomotion[c]	Walking speed	.39	5	Deere and Chown 2006
Fungal symbiont of lichen	Growth	Increase in area	.53	4	Sun and Friedmann 2005
Algal symbiont of lichen	Growth	Increase in area	−.82	7	Sun and Friedmann 2005
Fish	Growth[a]	Increase in mass	−.10	23	Asbury 2008
Arctic charr	Growth[a]	Increase in mass	−.62	11	Larsson et al. 2005
Trees	Photosynthesis	Net photosynthetic rate	.72	8	Gratani and Varone 2004
Trees	Photosynthesis	Net photosynthetic rate	−.18	8	Cunningham and Read 2002
Pea aphid	Development	Inverse of developmental period	−.66	5	Lamb et al. 1987
Endoparasites	Parasitization	Frequency of infection	.25	12	Grewal et al. 1994
Wasp	Parasitization	Frequency of infection	−.31	26	Carrière and Boivin 1997
Algae	Population growth	Doublings of cells per day	−.92	4	Eppley 1972
Actinobacteria	Population growth	Increase in optical density	−.85	6	Hahn and Pockl 2005
Water fleas	Population growth	Malthusian parameter (r)	−.69	29	Palaima 2002
Cyanobacteria	Population growth	Doublings of cells per day	.78	15	Miller and Castenholz 2000
Escherichia coli	Population growth	Malthusian parameter (r)	−.82	143	Knies et al. 2009
Bacteriophages	Population growth	Malthusian parameter (r)	−.93[d]	15	Knies et al. 2009
Insects	Population growth	Malthusian parameter (r)	−.50[d]	65	Frazier et al. 2006

Note. For each study, we report the specific measure of performance, the correlation between $1/kT_{opt}$ and ln P_{max}, and the number of taxa used to compute this correlation.

[a] Performance was adjusted for body size.

[b] Some taxa were omitted because optimal temperature was not resolved.

[c] Performance was averaged among acclimation treatments.

[d] Correlation coefficient was estimated from independent contrasts.

In general, warm-adapted taxa outperformed cold-adapted taxa (Fisher's $z = -0.72$, 95% confidence interval $= -0.21$ to -0.99). The size of the effect varied significantly among studies ($Q_{\text{total}} = 124.20$, df $= 20$, $P < 0.00001$), which likely resulted in part from our consideration of different performances. Studies of population growth yielded strong relationships between the optimal temperature and the maximal rate (Fisher's $z = -0.90$, 95% confidence interval $= -0.13$ to -1.18), whereas studies of other performances yielded weaker effects (Fig. 3). This result suggests that organisms can compensate for biochemical constraints on performance through adaptations at higher levels of organization (Angilletta et al. 2003) but cannot overcome constraints on fitness. Nevertheless, the relationship between the optimal temperature and the maximal rate of population growth was sometimes stronger or weaker than predicted by Savage et al. (2004). Thus, our meta-analysis of comparative studies supports the thermodynamic constraint hypothesis. Still, the wide range of thermodynamic effects, including some cases where colder appears better, generates doubt about whether this hypothesis describes a universal phenomenon.

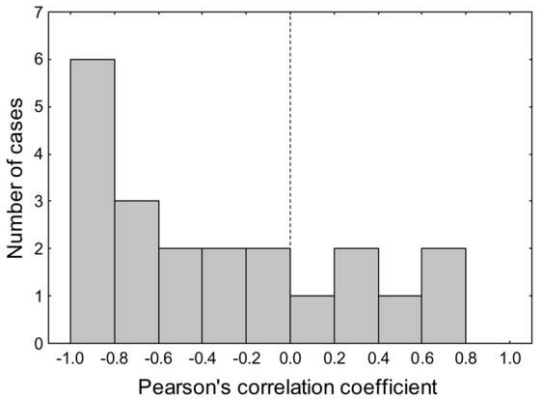

Figure 3. The majority of relationships between the optimal temperature for performance and the maximal performance support the thermodynamic constraint hypothesis. Because correlations were computed on an Arrhenius scale, a negative correlation indicates that hotter is better.

Quantitative Genetics

Quantitative genetics provides another approach to testing the thermodynamic constraint hypothesis. If the evolution of a lower optimal temperature necessarily reduces maximal performance, this relationship would be expressed as a genetic correlation (Arnold 1987). Specifically, we expect to see a positive genetic correlation between optimal temperature and maximal performance. A genetic correlation can be detected through artificial selection or a breeding experiment (Falconer 1989; Lynch and Walsh 1998); however, when performance can be measured only in a single thermal environment for any individual, one must use clones or siblings to estimate thermal sensitivities (Scheiner 2002).

To date, no researcher has examined the genetic variances and covariances associated with the thermal sensitivity of population growth, but some have done so for the thermal sensitivities of other performances. Two breeding experiments enable us to assess genetic correlations between the optimal temperature and the maximal performance. Gilchrist (1996) compared the thermal sensitivity of walking speed among families of parasitic wasps (*Aphidius ervi*). Similarly, Kingsolver et al. (2004) and Izem and Kingsolver (2005) compared the thermal sensitivity of growth rate among full-sib families of caterpillars (*Pieris rapae*). In each experiment, pairs of animals were randomly mated, full siblings were raised in controlled environments, and the thermal sensitivity of performance was compared among families. For this experimental design, the genetic correlation between two traits scales proportionally to the covariance among families (see Falconer 1989). Surprisingly, both studies failed to detect covariation among families that mirrored the covariation among populations and species revealed by our meta-analysis (see Table 1). In other words, neither study detected a correlation between the optimal temperature and the mean or maximal rate of performance. Additional estimates of genetic correlations would help to infer whether the patterns detected by intra- and interspecific comparisons reflect physical constraints on evolution.

Experimental Evolution

The relatively recent application of experimental evolution by physiologists (Garland and Rose 2009) provides new opportunities to test the thermodynamic constraint hypothesis. In some experiments, ancestral lines were subdivided and placed in several thermal environments, which caused their thermal physiology to diverge over many generations. If hotter is better, adaptation to an elevated temperature should result in enhanced performance at the new optimal temperature. Unfortunately, most of these experiments were not designed to estimate optimal temperatures (Huey et al. 1991; James and Partridge 1995) or were too short to produce significant shifts in this parameter (Gilchrist et al. 1997). Still, some valuable insights can be gleaned from experiments with viruses, bacteria, and flies.

Experimental evolution of viruses generated patterns supporting the thermodynamic constraint hypothesis. Holder and Bull (2001) subjected the bacteriophage G4, which was adapted to 37°C, to evolution at stressfully high temperatures. These researchers held the virus at 41.5°C for 50 serial transfers (~100 generations), followed by 50 more transfers at 44°C. Subsequently, Knies et al. (2006) measured growth rates of the ancestral and evolved lines at six temperatures ranging from 27° to 44°C. These researchers then used a relatively new statistical approach, referred to as template mode of variation (Izem and Kingsolver 2005), to analyze variation in thermal sensitivity. After 100 transfers, the evolved phage had a higher optimal temperature than the ancestral phage. Consistent with the thermodynamic constraint hypothesis, the evolved population also grew faster at its optimal temperature.

Experimental evolution of bacteria yielded a surprising pat-

tern of covariation between the optimal temperature and the maximal performance. Cooper et al. (2001) compared thermal sensitivities of population growth between ancestral lines of *Escherichia coli*, which grew best at 40°C, and selected lines that experienced 37°C for 20,000 generations. Not surprisingly, the optimal temperature of the selected lines decreased, such that their new optimum matched the temperature of the selective environment. Contrary to the thermodynamic constraint hypothesis, evolved lines grew faster at their low optimal temperature than did ancestral lines at their high optimal temperature (although this could reflect progressive adaptation to the artificial nutritional medium or the constant thermal regime). Furthermore, a study of mutational effects refuted a necessary link between the optimal temperature and the maximal performance; mutants of *E. coli* whose performance curves were shifted toward higher temperatures were not characterized by higher maximal rates of population growth (Mongold et al. 1999). The patterns uncovered by these experiments contrast the pattern detected among natural isolates of *E. coli* (Bronikowski et al. 2001), in which isolates with higher optimal temperatures grew faster (Knies et al. 2009). Hence, evidence of a thermodynamic constraint from a comparative study has been countered by evidence from an experimental study of the same species.

Experiments involving flies also tell conflicting stories about thermodynamic effects on population growth. Partridge et al. (1995) studied the evolution of thermal sensitivity in *Drosophila melanogaster* during 4 yr at 16.5° or 25°C. After this period, they scored the longevity of females and their lifetime production of offspring at 16.5° and 25°C. They found significant evidence of adaptation to temperature. Flies that had evolved at 16.5°C produced more offspring at 16.5°C than they did at 25°C; the opposite was true for flies that had evolved at 25°C. More to the point, lifetime fecundity was greatest for the low-temperature lines measured at low temperature, which superficially suggests that colder is better. Lifetime fecundity constitutes a reasonable estimate of fitness when a population remains relatively stable over time (Kozłowski 1993), as in the experiment conducted by Partridge et al. (1995). In another experiment, Santos (2007) allowed replicate populations of *Drosophila subobscura* to evolve at a constant temperature of 13°, 18°, or 22°C. He then measured the net fitness of flies from each line at all three temperatures; net fitness was estimated as the increase in genotypic frequency during one generation. Not only did the optimal temperature diverge among these lines, but so did the mean fitness. Consistent with the pattern commonly observed in comparative studies, flies that evolved at 22°C had the highest mean fitness, whereas flies that evolved at 13°C had the lowest. The different conclusions prompted by these two experiments could reflect incompatible estimates of Darwinian fitness or different potentials for biochemical adaptation.

Does a Universal Thermodynamic Constraint Really Exist?

The thermodynamic constraint hypothesis describes a universal thermal effect on the performance of organisms that results from the kinetics of enzymes. Comparisons of thermal physiology among populations or species qualitatively support the hypothesis, suggesting that hotter is usually better, even though the magnitude (and direction) of the thermodynamic effect varies greatly among traits and taxa. This conclusion is especially robust with respect to population growth rate, a common estimate of fitness. Despite this comparative evidence, genetic correlations between the optimal temperature and the maximal performance have not yet been demonstrated within populations (though few attempts have been made). Moreover, selection experiments have shown that a reduction in maximal performance need not accompany adaptation to low temperatures.

Several factors could account for the wide range of thermodynamic effects revealed by our meta-analysis. First, most studies of thermal sensitivity have focused on physiological performances (e.g., locomotion, growth, and development), which depend on many variables other than temperature. Uncontrolled variations in organismal and environmental conditions could alter the relationship between the optimal temperature and the maximal performance, especially in comparative studies. Second, estimates of optimal temperatures likely suffer from several sources of error, including errors resulting from inadequate sampling of the thermal range and statistical modeling of the performance curve (Angilletta 2006). Finally, adaptation could offset thermal effects on enzyme kinetics (Clarke 2006). In particular, an organism can enhance a performance by increasing the concentrations of relevant enzymes (reviewed by Somero 1995). Although this strategy would impose a trade-off by depleting resources available for other performances, such trade-offs would become evident only if one examined the thermal sensitivity of multiple performances (Angilletta et al. 2003). Nevertheless, these trade-offs would ultimately constrain the thermal sensitivity of fitness. Thus, we expect thermodynamic effects on performance to vary within bounds set by trade-offs. Moreover, we expect the best evidence for the thermodynamic constraint hypothesis to come from studies of population growth rate (or a more appropriate estimate of fitness), as we found in our meta-analysis.

Thermal Adaptation under Thermodynamic Constraints

If thermodynamic factors constrain the evolution of maximal performance, then these constraints might qualitatively influence the evolution of thermal physiology. Early models of thermal adaptation presumed that, all else being equal, cold-adapted genotypes could achieve the same fitness as warm-adapted genotypes (reviewed by Angilletta 2009). These models predict that, at an evolutionary equilibrium, the optimal temperature for performance should roughly equal the mean (or modal) body temperature (see Gilchrist 1995). A mismatch between the body temperature and the optimal temperature would impair performance and hence should reduce the fitness of an organism (Huey and Bennett 1987). Furthermore, the same assumption implies that an organism's body temperature should match the operative environmental temperature (sensu

Bakken 1992). A mismatch between the preferred body temperature and the mean environmental temperature would impose an unnecessary cost of thermoregulation (Huey and Slatkin 1976), because the organism would need to work to achieve its preferred temperature. Therefore, the traditional view implies that coadaptation would produce a close match among environmental temperature, body temperature, and the optimal temperature for performance. The existence of a thermodynamic effect invalidates the traditional view and might radically alter our perception of thermal adaptation. If a warm-adapted genotype achieves a greater fitness than a cold-adapted genotype, natural selection can favor large discrepancies among environmental temperature, body temperature, and optimal temperatures.

The potential mismatch between environmental temperature and body temperature was recognized decades ago when Hamilton (1973) invoked a thermodynamic constraint as a plausible stimulus for the evolution of endothermy. If the thermodynamic benefit of endothermy outweighs the energetic cost, one would expect the mean body temperature of an organism to exceed the mean environmental temperature. Of course, the cost of endothermy includes the energy required to produce insulation as well as heat, and this cost may be too high to favor endothermy in most species. Many debates have focused on the evolution of endothermy in birds and in mammals (reviewed by Hayes and Garland 1995; Koteja 2004; Angilletta 2009). Surprisingly, thermodynamic constraints on performance have not played a prominent role in these debates (but see Angilletta et al. 2010). Rather, the debates have focused on the relative roles of direct and indirect responses to selection in promoting the metabolism needed to elevate an organism's body temperature above its operative environmental temperature (Crompton et al. 1978; Bennett and Ruben 1979; Farmer 2000; Koteja 2000; Angilletta and Sears 2003). Perhaps researchers on both sides of the debate have taken for granted that organisms would derive a thermodynamic benefit from endothermy.

A thermodynamic constraint could also generate a mismatch between the mean body temperature and the optimal temperature for performance. Asbury and Angilletta modeled the optimal performance curve under the assumption that the maximal performance scaled positively with the optimal temperature (as shown in Fig. 2*C*; D. A. Asbury and M. J. Angilletta, unpublished manuscript). When body temperature varies little within generations, the predictions of the model do not deviate from those of a model without a thermodynamic constraint; specifically, selection favors an optimal temperature for performance that closely matches the mean body temperature (see Gilchrist 1995). But when body temperature varies greatly within generations, selection favors an optimal temperature for performance that exceeds the mean body temperature. Because of the thermodynamic effect, a mismatch can improve performance at the optimal temperature without impairing performance at the mean body temperature (Fig. 2*A*). The predicted mismatch scales according to the variation in body temperature. Consistent with this model, the optimal temperature for the locomotor performance of reptiles usually exceeds the preferred body temperature (Martin and Huey 2008).

In summary, thermodynamics might not only constrain the maximal performance of organisms, they might also impose novel selective pressures on thermoregulatory behavior and thermal physiology. These selective pressures would give priority to thermoregulation as a means of dealing with thermal heterogeneity, potentially simplifying our view of thermal adaptation (Angilletta et al. 2006). Of course, the specific evolutionary consequences would depend on the magnitude of the thermodynamic effect, the manner in which performance contributes to fitness, the life history of the organism, and the interactions among species (see Angilletta 2009). Given the mounting evidence for thermodynamic constraints, we encourage additional efforts to quantify thermodynamic effects on performance and to understand their evolutionary consequences.

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