

# Interactions and trade-offs among physiological determinants of performance and reproductive success

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**Synopsis** How an animal performs in its natural environment ultimately plays a key role in its reproductive success. While a number of studies have investigated how selection acts on performance-related traits, far fewer studies have examined the mechanisms responsible for variation in performance. Among mechanisms, variable morphology has received the most attention. Although physiological traits have received less attention, they are intrinsically related to performance and ultimately to reproductive success. We present a framework whereby investigators can link some basic physiological functions with organismal performance and ultimately with reproductive success. We propose that performance and ultimately reproductive success are strongly influenced by hormones, immune functions, and energetics. We further argue that no physiological function can be considered in isolation and thus our model emphasizes interactions and trade-offs both within each physiological function as well as among them. Some of the most commonly studied trade-offs are between reproduction and immune functions, with energetics as one of the key common currencies for these trade-offs. From an evolutionary perspective, the largest gaps in our knowledge lie in how these interactions and trade-offs influence reproductive success. We believe that a full understanding of how hormones, immune functions, and energetics influence performance traits related to reproduction and, ultimately, lifetime reproductive success requires recognition of the complex relationships, interactions, and trade-offs among these processes.

## Introduction

The ultimate goal for many studies in evolutionary biology is to understand the factors that contribute to an individual's fitness. Recently, many investigations have attempted to understand individual variation in reproductive success through investigations of performance (Kingsolver and Huey 2003; Irschick et al. 2008). Often these studies focus on male animals and attempt to discern if performance characters such as speed, endurance, or fighting ability can explain why some individuals are more successful than others in acquiring mates. As studies have begun to identify performance characters that are associated with reproductive success, interest in the morphological and physiological characters mediating these performance differences has emerged (Arnold 1983; Kingsolver and Huey 2003; Irschick et al. 2007; McGlothlin and Ketterson 2008). In this article we outline some of the physiological processes that must be considered when attempting to connect physiology with performance and reproductive success.

Why is it important to consider physiology when trying to understand performance? Much of the organismal basis for performance is fundamentally physiological. How fast or long an animal can run is hugely dependent on metabolic processes. Thus, individual variation in physiology has the potential to explain variation in performance. In a seminal work, Arnold (1983) identified the importance of considering morphology when trying to understand how selection acts on performance and fitness. His model emphasized linkages that connect phenotypic traits with performance and ultimately with reproductive success (Arnold 1983). However, performance is determined by more than just morphology and while Arnold's model did not discount physiology, it focused on morphological traits as determinants of performance. We know that variation in performance can occur because of differences in physiological function associated with morphology. For example, larger individuals with greater ability to perform may have higher testosterone levels than do smaller individuals

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(Husak et al. 2007). While the morphologist would focus on the differences in size among individuals, the physiologist would focus on the hormonal differences. In reality, morphology and physiology are not independent and often influence one another. As such, it is becoming clear that evolutionary ecologists need to consider both physiology and morphology in attempting to understand the mechanisms mediating individual variation in performance.

When considering how physiological function influences performance it is important to consider how selection will act on physiological traits. We propose that selection can act both directly and indirectly on physiological function. For example, production of testosterone must be maintained for proper growth and maturation of sperm (Norris 1997). In such a case, selection may act *directly* on testosterone levels or its function (e.g. receptors). However, selection may also act on a performance trait that is mediated by testosterone. For example, song production in birds is mediated, at least partially, by testosterone (Brenowitz 2002). Thus, when selection acts on song performance, it is *indirectly* acting on testosterone levels or its function. From an evolutionary perspective considering how selection acts both directly and indirectly upon physiological function is essential for understanding how such functions evolve.

A recent synthesis proposed a nexus between studies of life-history and physiology (Ricklefs and Wikelski 2002). The authors suggested that to understand variation in life history traits and its limitations, one must have an understanding of underlying physiological function. The physiology/life-history nexus has dramatically influenced both the way that evolutionary biologists think about mechanisms as well as the way that physiologists think about the evolution of physiological functions (Hau 2007). With our current article we propose a similar idea but substitute performance traits for life-history traits. So while the physiology/life-history nexus was used to explain variation in life-history traits, such as clutch size, our model can be used to explain the physiological basis for differences in performance. While our version is more proximate than the more ultimate aspects of the physiology/life-history nexus, we suggest that the integrative nature of both models is comparable and crucial to continuing to develop an understanding of organismal animal biology.

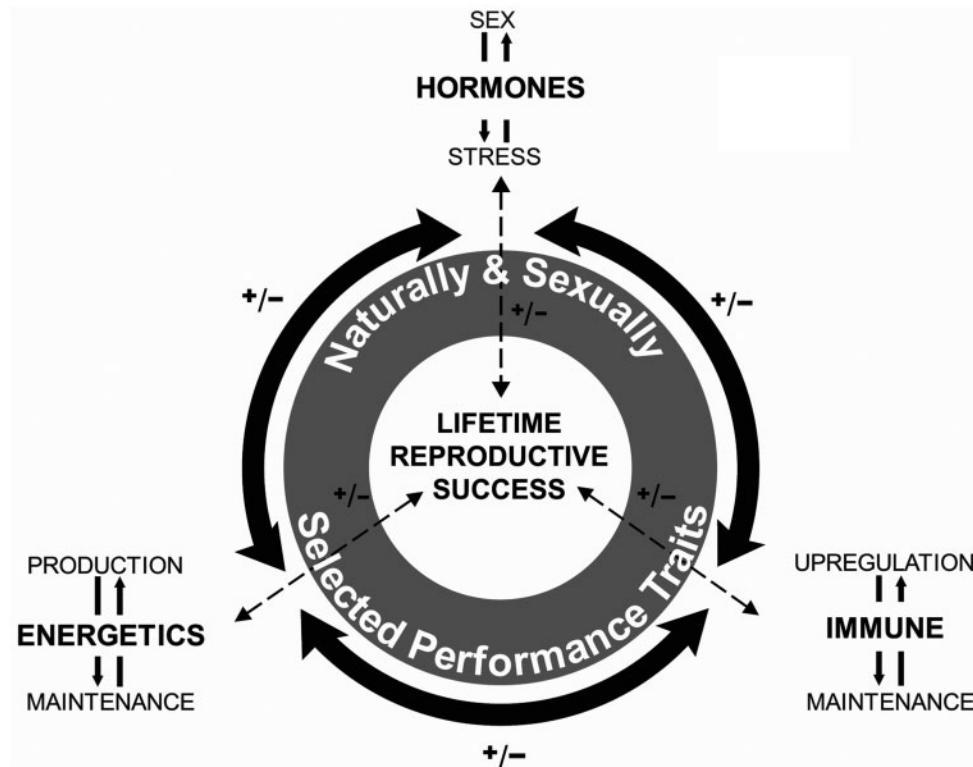
What are performance traits? Previous studies have described performance traits as ecologically relevant performance characteristics upon which selection can act (Huey and Stevenson 1979).

Typically these performance traits include characters such as sprint speed, endurance, and bite force that can be measured in a laboratory under controlled conditions (Irschick et al. 2008). Such studies of performance often do not include behaviors expressed in a reproductive context even though these are often determinants of reproductive success. Among performance traits that can strongly influence reproductive success we propose the inclusion of behaviors involved in attracting and/or defending mates and/or territories. We advocate the inclusion of such behaviors because there is little doubt that behaviors such as territorial aggression and courtship are crucial for gaining access to mates and thus maximizing reproductive success (Reid et al. 2005). A key difference between typical performance characteristics and reproductive behaviors is the type of selection that may act upon them. While behaviors such as sprint speed and endurance are typically, but not exclusively, under natural selection (ability to capture prey and avoid predators), reproductive and territorial behaviors are typically driven by sexual selection (intra-sexual competition and inter-sexual attraction). Regardless of the type of selection that acts upon them, we maintain that reproductive behaviors should be considered as performance characteristics that determine reproductive success.

### Goal of article

The primary goal of this article is to provide a framework that links vital physiological components that underpin performance traits important to reproduction, in a manner that permits a better understanding of the trade-offs among these physiological processes. This is an important topic for organismal biologists as many investigators are studying physiological functions or variation in reproductive success but few are trying to link the two through performance. By integrating reproductive success into studies of physiology and performance, we can better understand how selection is acting on performance and physiological traits. While performance and reproductive success have been reviewed before (Irschick et al. 2008), the incorporation of physiological mechanisms into the framework is a significant addition that will further our understanding of organismal form and function.

In addition to briefly describing some key conceptual issues, we present a comprehensive logistical framework to understand the relationships among physiological function, performance traits and reproductive success. We present this framework as



**Fig. 1** Conceptual diagram illustrating some of the key trade-offs and interactions that occur among physiological processes, ultimately influencing animal performance and reproductive success. Although each physiological process may have a direct (small dashed arrows) positive (+) or negative (–) influence on performance and reproduction, in most cases multiple physiological processes will interact to influence (bold peripheral arrows) an individual's fitness. Note that even within each physiological system, there are competing demands (e.g. energy for maintenance and production) and interactions among signals (e.g. different hormones).

a model (Fig. 1) that describes how we believe that physiological function is related to performance traits and to reproductive success. A key characteristic of our model is the emphasis on interactions. The interactions can occur between physiological processes (i.e., the outer ring of the figure; for example immune functions can be related to hormone levels) as well as between physiology and performance traits (e.g., sex steroids may affect aggressive displays which, in turn, results in changes in hormone levels). While many studies have investigated one or two of these three factors (physiology, performance, and reproductive success) few investigators have developed an understanding of the connectivity among all three. Often the gap in our knowledge occurs at linking variation in physiological function with reproductive success. For example, we might understand how hormones mediate a behavior or performance trait but we do not understand what this means for reproductive success. The theoretical model we propose provides the framework for investigators to develop testable hypotheses within a consistent framework to rectify this shortfall in knowledge.

## Physiology and performance

A recent paper suggested that studies of performance should adopt a “Functional Approach” towards understanding the hormonal mechanisms mediating performance characteristics (Irschick et al. 2007). We agree with that idea but propose that physiological function in general needs to be addressed, not just hormones. Even among hormones, the majority of interest has centered on androgens such as testosterone. Many aspects of hormonal function are determined by interactions and trade-offs with other physiological processes. If investigators focus exclusively on how hormones affect performance they risk ignoring the trade-offs, and thus the organismal context within which selection is acting. In this article we propose that the primary physiological functions that will be crucial for performance are hormones, immune functions, and energetics. We choose these three physiological functions largely because they have been demonstrated to have strong interactions amongst one-another and can influence performance. Certainly other physiological functions are also important for performance but have not

received as much attention and thus are not as easily incorporated into a conceptual framework. We use hormones in their most general sense. Certainly many chemical messengers can affect performance through a variety of mechanisms. Many hormones probably play important roles in performance, including those that influence metabolism, such as thyroid hormones, insulin, leptin, glucagon and others (Norris 1997). However, for simplicity we have chosen to focus on interactions between stress and sex steroids as two prime hormonal mediators of organismal performance. We include immune functions as an important mediator of performance because of its close interactions with the endocrine system (Nelson and Demas 1996) as well as with the energetic costs associated with maintaining and/or activating immune activity (Martin II et al. 2003). Lastly, we include energetics because energy is amongst the most important common currencies (along with time) important for the trade-offs among different physiological functions. Also, energy is a key determinant of aspects of organismal performance such as speed, endurance, and display rates. We propose that by considering these three broad physiological characters (hormones, immune functions, and energetics) together we can understand interactions and trade-offs among them and develop a more comprehensive view on how physiology affects performance.

### Hormones (sex and stress) and performance

There is good evidence that androgens can affect performance, especially in terms of behaviors associated with reproduction (Wingfield 1994, 2005). The identification of androgens as important mediators of the aggressive and reproductive behaviors of males emerged from some of the first endocrine studies and similar investigations continue today (Soma 2006). The role of androgens in mediating behaviors associated with reproduction has been modeled by the Challenge Hypothesis (Wingfield et al. 1990; Hirschenhauser et al. 2003; Goymann et al. 2007; Moore 2007). One of the key concepts of this hypothesis is the reciprocal nature of hormones and behavior: androgens can mediate aggressive behavior but aggressive behavior can also affect androgen levels. This relationship between androgens and reproductive behaviors is dependent on the mating system as well as on the degree of paternal care in the species. For example, socially monogamous species, in which males exhibit paternal care, are modeled to have a brief peak in testosterone at the beginning of the breeding season when mates are

selected and territories defined. The peaks in testosterone are associated the social interactions, challenges from other males, and mating opportunities with fertile females. At the other extreme, polygynous species in which males do not care for young are modeled to have elevated levels of testosterone throughout the extended breeding season, but without peaks. In addition to the role of androgens in behavior, there is ample evidence that androgens can affect skeletal musculature of importance to sprinting and endurance (see Husak and Irschick 2009). In sum, androgens can affect multiple aspects of performance and behavior.

Glucocorticoid stress hormones traditionally have been thought of in terms of survival (Sapolsky 1990) but more recently have been implicated as potentially important mediators of performance (Moore and Jessop 2003; Romero 2004). In response to a stressful or energetically demanding situation, vertebrates typically activate the hypothalamic-pituitary-adrenal axis which results in the release of glucocorticoid stress hormones into the circulation (i.e., the hormonal stress response). These hormones are typically thought to mobilize energy stores and suppress processes unnecessary for immediate survival, such as reproduction, until conditions improve (Wingfield and Sapolsky 2003). The stress response thus should increase the immediate odds of survival of the individual, perhaps at the expense of immediate reproductive success. The potential role of glucocorticoids in performance largely comes from their role in the mobilization of energy. Many performance characteristics are energetically expensive (i.e., calling in frogs; see Leary 2009) and thus dependent on the ability of the individual to mobilize and utilize energy.

The thought that stress simply suppresses reproduction (Selye 1936, 1956) had been rather well accepted for many years (Greenberg and Wingfield 1987). Now we know that in some situations, glucocorticoids and sex steroids are positively related and glucocorticoids can be elevated during periods of breeding (Moore et al. 2000; Romero 2002; Moore and Jessop 2003). In cases in which finding or defending a mate is energetically costly, it is predicted that glucocorticoids facilitate, rather than suppress, reproduction (Moore and Jessop 2003; Husak and Moore 2008). The facilitation of reproduction and performance are probably occurring through the energy-mobilizing role of glucocorticoid hormones. More broadly, these recent studies have demonstrated that it is critical to consider the context in which stress hormones will act if one is to understand their influence on reproduction and



performance. The same hormone can have different actions at different plasma levels, or have different actions at the same plasma level depending on context (e.g. reproductive condition). The great variety of actions that glucocorticoids can mediate are at least partly due to plasma-binding proteins and the variety of receptors through which the hormones can act (Breuner et al. 2003).

It is also becoming evident that stress hormones can be a target of sexual selection in addition to the more accepted target of natural selection (Husak and Moore 2008). In terms of mate choice, a few studies have shown that individuals can exhibit preferences for mates depending on the mate's glucocorticoid levels (Roberts et al. 2007a; Roulin et al. 2008; Wada et al. 2008). This appears to occur because stress hormones can be key mediators of many condition-dependent, sexually selected traits that serve as honest signals of mate quality. The mechanisms by which sexually selected traits are mediated by stress hormones is often not clear, but it is apparent that some of the effects may be occurring through performance.

### **Energetics (maintenance versus production) and performance**

Because virtually everything an animal does physiologically and behaviorally requires energy, many evolutionary ecologists have advocated energy as the common currency by which important allocation decisions and trade-offs can be quantified. Indeed, much of life-history theory is based upon the differential allocation of energy to competing functions such as maintenance of the soma and production of new tissues for processes including growth and reproduction (Congdon 1982). Because the amount of energy an individual can harvest is finite, and different foods vary in nutritional content, increased allocation of energy to one component of an animal's energy budget often requires reduced allocation to others. Thus, in the absence of increased assimilation of energy, energetically costly performance activities should constrain allocation of energy to other processes.

Many performance traits associated with reproduction and territoriality are believed to be energetically costly, yet relatively few of these costs in energy have been rigorously quantified. Sustained locomotion, intense breeding and territorial displays, and aspects of male-male combat should all carry significant costs in energy. Among the best-studied examples is calling performance in anuran amphibians, a behavioral trait that is critical for attracting

mates. Many anurans engage in prolonged periods of vocalization fueled primarily by aerobic metabolism, and resulting in significant expenditures of energy and loss of time (another important common currency) for other activities. The results of several studies suggest that this important performance trait is among the most energetically demanding activities known in vertebrates (Taigen and Wells 1985; Wells 1996; Prestwich et al. 1989). Because of these high costs in energy, energetic constraints have been invoked as explanations for duration of choruses (Bertram et al. 1996; Smith et al. 2003) and the evolution of condition-dependent alternative reproductive tactics in male anurans (McCauley et al. 2000; Leary et al. 2004, 2005). It is reasonable to postulate that other trade-offs, such as reduced allocation of energy towards immune defenses, may occur in species that engage in these intensive activities to attract mates (see below). From an evolutionary perspective, however, the fitness advantages of paying these high energy costs for performance must outweigh their disadvantages. We assert that direct quantification of these trade-offs in energy will be a significant advancement in the framework proposed here, as well as for sexual selection theory.

### **Interactions and trade-offs**

It is crucial to consider interactions among hormones, immune functions, and energetics if one is to understand how physiology affects performance and reproductive success. An important aspect of this is considering whether these interactions require trade-offs. As both reproduction and immune functions are costly activities, if available energy is finite then it is likely that trade-offs exist between the systems. If trade-offs do exist, energy could be an important currency used to quantify them.

### **Interactions of hormones and energy**

Reproduction is an inherently costly activity, and elevated plasma levels of hormones often serve as an underlying mechanism that drives reproductive, as well as other, energy expenditures. For example, elevated testosterone increases cellular metabolism (Sato et al. 2008) and can ultimately improve growth and muscle mass (Yanase et al. 2008). Although rapid growth and larger body size may improve size-dependent performance characters and reproductive success in some cases, accruing additional tissue also increases overall maintenance costs for the individual. In addition, exogenous testosterone can increase feeding and activity in

birds (Wikelski et al. 1999; Lynn et al. 2000) and aggressive behaviors in lizards (Marler et al. 1995). Such changes in activity should be associated with increased energetic costs, but studies quantifying overall energy expenditures by animals with elevated testosterone have produced conflicting results. In some cases, increased testosterone increased daily energy expenditure (Marler et al. 1995) but in other cases it did not (Lynn et al. 2000). Likewise, some studies examining how testosterone influences individual components of the energy budget, such as resting, basal, or standard metabolic rate, have produced very different outcomes (Deviche 1992; Marler et al. 1995; Wikelski et al. 1999; Buttemer and Astheimer 2000; Buchanan et al. 2001; Buttemer et al. 2008).

Similar to the conflicting literature on testosterone, inconsistencies exist in the literature regarding the effects of glucocorticoids on expenditures of energy. This is particularly surprising because in the literature, increased plasma levels of glucocorticoids are usually assumed to pose a significant energetic cost to the animal. In fact, many current theories of stress rely heavily on this idea (Wingfield et al. 1998; McEwen and Wingfield 2003). The supposition of high energetic costs of glucocorticoids has strong theoretical support in light of the fact that the primary role of glucocorticoids is thought to be the regulation of intermediary metabolism and thus the mobilization of energy. However, available evidence provides mixed support for this theoretical assumption (DuRant et al. 2008; Romero et al. 2009). For example, exogenous glucocorticoids at physiological levels are known to increase metabolic rate of lizards (DuRant et al. 2008) and fish (Morgan and Iwama 1996), but to decrease resting metabolism at night in birds (Buttemer et al. 1991). Because in many energy-demanding circumstances animals modify their behavior and activity patterns while simultaneously up-regulating and down-regulating competing physiological processes, predicting overall changes in energy expenditure may be difficult. For example, lizards chronically exposed to exogenous glucocorticoids exhibited reduced resting metabolism but improved locomotor performance (Miles et al. 2007). Thus, the effect of glucocorticoids on the energetics of whole animals depends on the species and context of the study, but studies examining the potential compensatory mechanisms that offset the costs of up-regulated intermediary metabolism at the whole-animal level have rarely been performed.

Taken together it is clear that our overall understanding of the effects of hormones on the energy

expenditure of animals in ecological settings is still rudimentary. To further complicate matters, multiple hormones often interact to produce behavioral and reproductive outcomes. We are unaware of bioenergetic studies that have simultaneously manipulated androgens and glucocorticoids, but it is increasingly clear that such studies are necessary for understanding how glucocorticoids facilitate energetically costly performance traits such as reproductive displays [see section: Hormones (sex and stress) and performance]. Regardless of whether single or multiple hormones are being manipulated, future studies should simultaneously quantify multiple aspects of an animal's energy budget to determine how differential allocation to one compartment of an energy budget detracts from other compartments. In many cases it will also be necessary to monitor behavioral changes, since slight modifications in activity can have large energetic consequences. By addressing these problems in an integrative framework, it may be possible to understand the compensatory responses that allow animals to maintain energy balance when faced with energetic challenges, such as testosterone-induced changes in reproductive behavior and performance. Importantly, these trade-offs appear to be context-dependent, so study systems should be carefully selected and described so that comparisons among studies might ultimately lead to useful generalizations.

#### Interactions of hormones and immune functions

Much of the recent work investigating interactions between immune functions and hormones has been based on the immunocompetence handicap hypothesis (Folstad and Karter 1992). This hypothesis posits that elevated testosterone levels mediate a trade-off between expression of testosterone-enhancing sexual traits and testosterone-suppressing immune functions. In such a case, testosterone-mediated traits are considered to serve as honest signals of male quality. While this hypothesis is attractive, the tests of it have produced inconsistent results. A review and meta-analysis of the studies that tested the immunocompetence handicap hypothesis found mixed support and suggested that some of the discrepancies depended on whether the studies were observational or experimental (Roberts et al. 2004). As an example, in superb fairy-wrens (*Malurus cyaneus*) experimental treatment with testosterone suppressed immune function (Peters 2000). However, observational data of free-living individuals showed elevated levels of endogenous testosterone were associated with enhanced immune function

(Peters 2000). In addition, in a study of red jungle fowl (*Gallus gallus*), numbers of immune cells were positively related to testosterone levels rather than the predicted negative relationship (Zuk et al. 1995). There is some evidence for negative effects of testosterone on measures of parasitism (Malo et al. 2009). Other studies have suggested that the immunocompetence handicap hypothesis is not simply associated with testosterone but that interactions with glucocorticoids are important (Roberts et al. 2004). In such a case, elevated sex steroids may be accompanied by elevated glucocorticoids which may be immunosuppressive (Owen-Ashley et al. 2004). However, support for this version is also not universal (Roberts et al. 2007b). It is evident that overall support for the immunocompetence handicap hypothesis is unclear (Roberts et al. 2004).

Traditionally glucocorticoids were thought to be immunosuppressive, with the general idea being that immune functions could be suppressed until the stressor has subsided (Wingfield et al. 1998). Studies in some lizards have supported the idea of stress and glucocorticoids as being immunosuppressive (Oppliger et al. 1998) but studies in other lizards have not supported this interpretation (Hanley and Stamps 2002). What is becoming clear is that the immunosuppressive activity of glucocorticoids is not universal (Martin II et al. 2005). Some studies even suggest that acute elevations of glucocorticoids may, in fact, be immunoenhancing (Dhabhar and McEwen 1999).

As a response to the conflicting data on interactions between hormones and immune functions, an alternative immunoredistribution hypothesis has emerged (Braude et al. 1999). The immunoredistribution hypothesis posits that immune cells are temporarily shifted to compartments where they are likely to be more useful in response to some stimuli, and that hormones could mediate these shifts (Braude et al. 1999). The immunoredistribution hypothesis is inherently more complicated and difficult to test than is the immunocompetence hypothesis but potentially has more explanatory power. Certainly more studies need to be conducted on interactions between hormones and immune functions if we are to elucidate consistent relationships and understand how these are related to reproductive success (Zuk 1996).

### Interactions of immune functions and energy

The immune system is believed to be an energetically costly physiological system to maintain and utilize.

Both innate and acquired immunity require energy and nutrients (e.g. protein) and in some cases, the costs of up-regulating these defenses has been shown to be substantial (Demas et al. 1997; Wakelin 1997; Buttgerit et al. 2000; Lochmiller and Deerenberg 2000; Ots et al. 2001; Martin II et al. 2003; Demas 2004). For example, mice injected with keyhole limpet hemocyanin (KLH), a protein that generates a robust antigenic response without other adverse side-effects, exhibited a 30% increase in metabolic rate compared to controls (Demas et al. 1997). Energetic reactions such as this, especially if maintained over the course of days, should incur significant energy costs. To illustrate this, Martin II et al. (2003) subjected house sparrows (*Passer domesticus*) to a single challenge with phytohaemagglutinin (PHA), a commonly used mitogen that stimulates cell-mediated immunity and a local inflammatory response. The challenge resulted in a significant increase in metabolism that was sustained for >1 day, resulting in energy expenditure equivalent to producing half an egg. There are likely many more energetically costly cases of mounting immune defenses, especially considering other aspects of integrated immune reactions such as fever and repairing damaged tissue that carry additional energetic costs.

The energetic and nutritional challenges associated with the immune system may place significant constraints on an animal's performance and reproductive success. In some cases, organisms may overcome the simultaneous competing demands of energetically costly activities such as immunity and reproduction by assimilating additional energy (i.e. eating more or more nutritional foods) from the environment. However, time constraints and the finite nature of resources may limit this possibility in ecological settings. Even under optimal resource conditions, nutritional demands may simply be too high for animals to fuel these competing demands. For example, Derrenberg et al. (1997) demonstrated that reproductively active zebra finches that were injected with sheep red blood cells (SRBC), a commonly used antigenic challenge, were incapable of improving their humoral response even with abundant supplementary provisions of protein-enriched food. This study supports the notion that other portions of an animal's energy budget may be penalized for prioritizing allocation of energy to immunity and/or to reproductive processes. Because many performance traits can be size-dependent and/or condition-dependent, it is certainly plausible that key performance characters that influence

reproductive success could be compromised by the energetic demands of immune responses.

### Hormones–energetics–immune functions

The ecological context of endocrine function, energetics, and immune functions is an active area of research. However, relatively few studies have integrated the three factors and attempted to understand interactions and trade-offs among them. Boughton et al. (2007) described energetic trade-offs between reproduction and immune functions in male Japanese quail with castrated males having lower metabolic rates and increased immune responsiveness. In another study, implantation of testosterone resulted in a decrease in one measure of immune functions in the common wall lizard (*Podarcis muralis*) but not a decrease in the number of ectoparasites or hemoparasites (Oppliger et al. 2004). Interestingly, the same implants did not affect resting metabolic rate but did enhance mean metabolic rate, presumably because of increased activity (Oppliger et al. 2004). These studies suggest that trade-offs do exist between hormones and immune functions and that energetics are an important currency for understanding the trade-offs. However, usually we have a poor understanding of what these interactions and trade-offs mean for performance and reproductive success.

In a series of integrative studies, French and colleagues investigated interactions among reproduction and wound healing in terms of energetic trade-offs in a lizard. Wound healing has the advantage of being a holistic measure of animal immune functions that is relevant to the challenges that an animal faces in ecological settings. In ornate tree lizards (*Urosaurus ornatus*), individuals exposed to stressful conditions had slower healing of wounds than did controls (French et al. 2006). In addition, wound healing varied with reproductive stage in both males and females (French and Moore 2008). Interestingly, the apparent trade-off between immune functions and reproduction in this species is facultative and based on energetics. In females, immune functions can suppress reproduction when energy (food supply) is limited (French et al. 2007b). Conversely, experimentally increased reproductive investment (by stimulating vitellogenesis) resulted in suppressed immune functions (French et al. 2007a). While this series of studies nicely illustrated the trade-offs among immune functions, hormones, and energetics, we do not yet understand the implications of these tradeoffs for performance and ultimately for reproductive success.

### Conclusions and future directions

Our conceptual model (Fig. 1) presents a holistic framework from which to investigate, and hopefully understand, how physiological function mediates performance characters that can influence reproductive success. Currently many studies are addressing some of these relationships but few systematically test the connectivity of all aspects of the model. The single biggest gap in our knowledge is linking how physiological function is related to performance traits and ultimately to reproductive success. This gap is probably a result of divergent interests between classical physiologists and evolutionary ecologists. While evolutionary ecologists have attempted to understand how selection acts, physiologists have been interested in describing basic function. Thus, we emphasize the need for a more holistic understanding of how variation in reproductive success is mediated by physiological function. Furthermore, physiological function, performance, and reproductive success can vary over ontogeny, emphasizing the need to consider both fecundity and longevity (lifetime reproductive success) within this conceptual framework.

The second focus of future research needs to be on understanding interactions and trade-offs among physiological characters and how these affect performance. This is a lofty goal and certainly requires a substantial number of both observational and experimental studies. It is abundantly clear that interactions and trade-offs occur among various hormones, different arms of the immune system, and competing portions of the animal's energy budget. Further, there are interactions among these three broad physiological functions. When investigators are interested in understanding how performance characters are physiologically mediated there is a temptation to look at hormones (Irschick et al. 2007). We see this as a first step and propose that investigating interactions and trade-offs with other physiological factors as logical continuations. We do not want to diminish the importance of unifacted studies but want to emphasize that the conclusions that can be drawn from such studies will be maximized when successive studies build upon each other in an integrative fashion.

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## References

- Arnold SJ. 1983. Morphology, performance and fitness. *Am Zool* 23:347–61.
- Bertram S, Berrill M, Nol E. 1996. Male mating success and variation in chorus attendance within and among breeding seasons in the gray treefrog (*Hyla versicolor*). *Copeia* 1996:729–34.
- Boughton RK, Bridge ES, Schoech SJ. 2007. Energetic trade-offs between immunity and reproduction in male Japanese quail (*Coturnix coturnix*). *J Exp Zool* 307A:479–87.
- Braude S, Tang-Martinez Z, Taylor GT. 1999. Stress, testosterone, and the immunoredistribution hypothesis. *Behav Ecol* 10:345–50.
- Brenowitz EA. 2002. Birdsong: integrating physics, physiology, and behavior. *J Comp Physiol A* 188:827–8.
- Breuner CW, Orchinik M, Hahn TP, Meddle SL, Moore IT, Owen-Ashley NT, Sperry TS, Wingfield J. 2003. Differential mechanisms for regulation of the stress response across latitudinal gradients. *Am J Physiol Regulat Integr Comp Physiol* 285:R594–600.
- Buchanan KL, Evans MR, Goldsmith AR, Bryant DM, Rowe LV. 2001. Testosterone influences basal metabolic rate in male house sparrows: a new cost of dominance signalling? *Proc Roy Soc B* 268:1337–44.
- Buttemer WA, Astheimer LB. 2000. Testosterone does not affect basal metabolic rate or blood parasite load in captive male White-plumed Honeyeaters *Lichenostomus penicillatus*. *J Avian Biol* 31:479–88.
- Buttemer WA, Astheimer LB, Wingfield JC. 1991. The effect of corticosterone on standard metabolic rates of small passerine birds. *J Comp Physiol B Biochem Syst Environ Physiol* 161:427–31.
- Buttemer WA, Warne S, Bech C, Astheimer LB. 2008. Testosterone effects on avian basal metabolic rate and aerobic performance: Facts and artefacts. *Comp Biochem Physiol A Mol Integr Physiol* 150:204–10.
- Buttgereit F, Burmester GR, Brand MD. 2000. Bioenergetics of immune functions: fundamental and therapeutic aspects. *Immunol Today* 21:192–9.
- Congdon JD, Dunham AE, Tinkle DW. 1982. Energy budgets and life histories of reptiles. In: Gans C, Pough H, editors. *Biology of the reptilia*. London: Academic Press. p. 233–71.
- Deerenberg C, Arpanius V, Daan S, Bos N. 1997. Reproductive effort decreases antibody responsiveness. *Proc Roy Soc Lond Ser B Biol Sci* 264:1021–9.
- Demas GE. 2004. The energetics of immunity: a neuro-endocrine link between energy balance and immune function. *Hormones Behav* 45:173–80.
- Demas GE, Chefer V, Talan MI, Nelson RJ. 1997. Metabolic costs of mounting an antigen-stimulated immune response in adult and aged C57BL/6J mice. *Am J Physiol Regulat Integr Comp Physiol* 273:R1631–7.
- Deviche P. 1992. Testosterone and opioids interact to regulate feeding in a male migratory songbird. *Hormones Behav* 26:394–405.
- Dhabhar FS, McEwen BS. 1999. Enhancing versus suppressive effects of stress hormones on skin immune function. *Proc Natl Acad Sci USA* 96:1059–64.
- DuRant SE, Romero LM, Talent LG, Hopkins WA. 2008. Effect of exogenous corticosterone on respiration in a reptile. *Gen Comp Endocrinol* 156:126–33.
- Folstad A, Karter AJ. 1992. Parasites, bright males and the immunocompetence handicap. *Am Natural* 139:603–22.
- French SS, DeNardo DF, Moore MC. 2007a. Trade-offs between the reproductive and immune systems: facultative responses to resources or obligate responses to reproduction. *Am Natural* 170:79–89.
- French SS, Johnston GIH, Moore MC. 2007b. Immune activity suppresses reproduction in food-limited female tree lizards *Urosaurus ornatus*. *Funct Ecol* 21:1115–22.
- French SS, Matt KS, Moore MC. 2006. The effects of stress on wound healing in male tree lizards (*Urosaurus ornatus*). *Gen Comp Endocrinol* 145:128–32.
- French SS, Moore MC. 2008. Immune function varies with reproductive stage and context in female and male tree lizards, *Urosaurus ornatus*. *Gen Comp Endocrinol* 155:148–56.
- Goymann W, Landys MM, Wingfield JC. 2007. Distinguishing seasonal androgen responses from male–male androgen responsiveness—revisiting the Challenge Hypothesis. *Hormones Behav* 51:463–76.
- Greenberg N, Wingfield J. 1987. Stress and reproduction: reciprocal relationships. In: Norris DO, Jones RE, editors. *Hormones and reproduction in fishes, amphibians, and reptiles*. New York: Plenum Press. p. 461–503.
- Hanley KA, Stamps JA. 2002. Does corticosterone mediate bidirectional interactions between social behaviour and blood parasites in the juvenile black iguana. *Ctenosaura similis*? *Anim Behav* 63:311–22.
- Hau M. 2007. Regulation of male traits by testosterone: implications for the evolution of vertebrate life histories. *BioEssays* 29:133–44.
- Hirschenhauser K, Winkler H, Oliveira RF. 2003. Comparative analysis of male androgen responsiveness to social environment in birds: the effects of mating system and paternal incubation. *Hormones Behav* 43:508–19.
- Huey RB, Stevenson RD. 1979. Integrating thermal physiology and ecology of ectotherms: a discussion of approaches. *Am Zool* 19:357–66.

- Husak JF, Irschick DJ. 2009. Steroid use and human performance: lessons for integrative biologists. *Integr Comp Biol*, doi:10.1093/icb/015.
- Husak JF, Irschick DJ, Meyers JJ, Lailvaux SP, Moore IT. 2007. Hormones, sexual signals, and performance of green anole lizards (*Anolis carolinensis*). *Hormones Behav* 52:360–7.
- Husak JF, Moore IT. 2008. Stress hormones and mate choice. *Trends Ecol Evol* 23:532–4.
- Irschick DJ, Herrel A, Vanhooydonck B, Van Damme R. 2007. A functional approach to sexual selection. *Funct Ecol* 21:621–6.
- Irschick DJ, Meyers JJ, Husak JF, Le Gaillard J-F. 2008. How does selection operate on whole-organism functional performance capacities? A review and synthesis. *Evol Ecol Res* 10:177–96.
- Kingsolver JG, Huey RB. 2003. Introduction: the evolution of morphology, performance and fitness. *Integr Comp Biol* 43:361–6.
- Leary CJ. 2009. Hormones and acoustic communication in anuran amphibians. *Integr Comp Biol*, doi:10.1093/icb/icp027.
- Leary CJ, Fox DJ, Shepard DB, Garcia AM. 2005. Body size, age, growth and alternative mating tactics in toads: satellite males are smaller but not younger than calling males. *Anim Behav* 70:663–71.
- Leary CJ, Jessop TS, Garcia AM, Knapp R. 2004. Steroid hormone profiles and relative body condition of calling and satellite toads: implications for proximate regulation of behavior in anurans. *Behav Ecol* 15:313–20.
- Lochmiller RL, Deerenberg C. 2000. Trade-offs in evolutionary immunology: just what is the cost of immunity? *OIKOS* 88:87–98.
- Lynn SE, Houtman AM, Weathers WW, Ketterson ED, Nolan V. 2000. Testosterone increases activity but not daily energy expenditure in captive male dark-eyed juncos, *Junco hyemalis*. *Anim Behav* 60:581–7.
- Malo AF, Roldan ERS, Garde JJ, Soler AJ, Vicente J, Gortazar C, Gomendio M. 2009. What does testosterone do for red deer males? *Proc Roy Soc B* 276:971–80.
- Marler CA, Walsberg G, White ML, Moore M. 1995. Increased energy-expenditure due to increased territorial defense in male lizards after phenotypic manipulation. *Behav Ecol Sociobiol* 37:225–31.
- Martin II LB, Gilliam J, Han P, Lee K, Wikelski M. 2005. Corticosterone suppresses cutaneous immune function in temperate but not tropical House Sparrows, *Passer domesticus*. *Gen Comp Endocrinol* 140:126–35.
- Martin II LB, Scheuerlein A, Wikelski M. 2003. Immune activity elevates energy expenditure of house sparrows: a link between direct and indirect costs? *Proc Roy Soc B* 270:153–8.
- McCauley SJ, Bouchard SS, Farina BJ, Isvaran K, Quader S, Wood DM, St Mary CM. 2000. Energetic dynamics and anuran breeding phenology: insights from a dynamic game. *Behav Ecol* 11:429–36.
- McEwen BS, Wingfield JC. 2003. The concept of allostasis in biology and biomedicine. *Hormones Behav* 43:2–15.
- McGlothlin JW, Ketterson ED. 2008. Hormone-mediated suites as adaptations and evolutionary constraints. *Philos Trans Roy Soc B* 363:1611–20.
- Miles DB, Calsbeek R, Sinervo B. 2007. Corticosterone, locomotor performance, and metabolism in side-blotched lizards (*Uta stansburiana*). *Hormones Behav* 51:548–54.
- Moore IT. 2007. Advancing the challenge hypothesis. *Hormones Behav* 51:461–2.
- Moore IT, Jessop TS. 2003. Stress, reproduction, and adrenocortical modulation in amphibians and reptiles. *Hormones Behav* 43:39–47.
- Moore IT, Lerner JP, Lerner DT, Mason RT. 2000. Relationships between annual cycles of testosterone, corticosterone, and body condition in male red-spotted garter snakes, *Thamnophis sirtalis concinnus*. *Physiol Biochem Zool* 73:307–12.
- Morgan JD, Iwama GK. 1996. Cortisol-induced changes in oxygen consumption and ionic regulation in coastal cutthroat trout (*Oncorhynchus clarki clarki*) parr. *Fish Physiol Biochem* 15:385–94.
- Nelson RJ, Demas GE. 1996. Seasonal changes in immune function. *Quart Rev Biol* 71:511–48.
- Norris DO. 1997. Vertebrate endocrinology. San Diego: Academic Press.
- Oppliger A, Clobert J, Locomte J, Lorenzon P, Boudjemadi K, John-Alder HB. 1998. Environmental stress increases the prevalence and intensity of blood parasite infection in the common lizard *Lacerta vivipara*. *Ecol Lett* 1:129–38.
- Oppliger A, Giorgi MS, Conelli A, Nembrini M, John-Alder HB. 2004. Effect of testosterone on immunocompetence, parasite load, and metabolism in the common wall lizard (*Podarcis muralis*). *Can J Zool* 82:1713–9.
- Ots I, Kerimov AB, Ivankina EV, Ilyina TA, Horak P. 2001. Immune challenge affects basal metabolic activity in wintering great tits. *Proc Roy Soc Lond Ser B Biol Sci* 268:1175–81.
- Owen-Ashley NT, Hasselquist D, Wingfield JC. 2004. Androgens and the immunocompetence handicap hypothesis: unraveling direct and indirect pathways of immunosuppression in song sparrows. *Am Natural* 164:490–505.
- Peters A. 2000. Testosterone treatment is immunosuppressive in superb fairy-wrens, yet free-living males with high testosterone are more immunocompetent. *Proc Roy Soc B* 267:883–9.
- Prestwich KN, Brugger KE, Topping M. 1989. Energy and communication in 3 species of hylid frogs- power input, power output and efficiency. *J Exp Biol* 144:53–80.
- Reid JM, Arcese P, Cassidy ALEV, Hiebert SM, Smith JNM, Stoddard PK, Marr AB, Keller LF. 2005. Fitness correlates of song repertoire size in free-living song sparrows (*Melospiza melodia*). *Am Natural* 165:299–310.

- Ricklefs RE, Wikelski M. 2002. The physiology/life-history nexus. *Trends Ecol Evol* 17:462–3.
- Roberts ML, Buchanan KL, Bennett ATD, Evans MR. 2007a. Mate choice in zebra finches: does corticosterone play a role? *Anim Behav* 74:921–9.
- Roberts ML, Buchanan KL, Evans MR. 2004. Testing the immunocompetence handicap hypothesis: a review of the evidence. *Anim Behav* 68:227–39.
- Roberts ML, Buchanan KL, Hasselquist D, Evans MR. 2007b. Effects of testosterone and corticosterone on immunocompetence in the zebra finch. *Hormones Behav* 51:126–34.
- Romero LM. 2002. Seasonal changes in plasma glucocorticoid concentrations in free-living vertebrates. *Gen Comp Endocrinol* 128:1–24.
- Romero LM. 2004. Physiological stress in ecology: lessons from biomedical research. *Trends Ecol Evol* 19:249–55.
- Romero LM, Dickens MJ, Cyr NE. 2009. The reactive scope model- a new model integrating homeostasis, allostasis, and stress. *Hormones Behav* 55:375–89.
- Roulin A, Almasi B, Rossi-Pedruzzi A, Ducrest A-L, Wakamatsus K, Miksik I, Blount JD, Jenni-Eiermann S, Jenni L. 2008. Corticosterone mediates the condition-dependent component of melanin-based coloration. *Anim Behav* 75:1351–8.
- Sapolsky RM. 1990. Stress in the wild. *Sci Am* 262:116–23.
- Sato K, Iemitsu M, Aizawa K, Ajisaka R. 2008. Testosterone and DHEA activate the glucose metabolism-related signaling pathway in skeletal muscle. *Am J Physiol Endocrinol Metab* 294:E961–8.
- Selye H. 1936. A syndrome produced by diverse nocuous agents. *Nature* 2003:32.
- Selye H. 1956. *The stress of life*. New York: McGraw-Hill.
- Smith MJ, Withers PC, Roberts JD. 2003. Reproductive energetics and behavior of an Australian myobatrachid frog *Crinia georgiana*. *Copeia* 138:248–54.
- Soma KK. 2006. Testosterone and aggression: Berthold, birds and beyond. *J Neuroendocrinol* 18:543–51.
- Taigen TL, Wells KD. 1985. Energetics of vocalization by an anuran amphibian (*Hyla versicolor*). *J Comp Physiol B Biochem Syst Environ Physiol* 155:163–70.
- Wada H, Salvante KG, Stables C, Wagner E, Williams TD, Breuner CW. 2008. Adrencortical responses in zebra finches (*Taeniopygia guttata*): individual variation, repeatability, and relationship to phenotypic quality. *Hormones Behav* 53:472–80.
- Wakelin D. 1997. Parasites and the immune system – conflict or compromise? *Bioscience* 47:32–40.
- Wells KD, Taigen TL, O'Brien J. 1996. The effect of temperature on calling energetics of the spring peeper (*Pseudacris crucifer*). *Amphibia Reptilia* 17:149–58.
- Wikelski M, Lynn S, Breuner CW, Wingfield JC, Kenagy GJ. 1999. Energy metabolism, testosterone and corticosterone in white-crowned sparrows. *J Comp Physiol A* 185:463–70.
- Wingfield JC. 1994. Control of territorial aggression in a changing environment. *Psychoneuroendocrinology* 19:709–21.
- Wingfield JC. 2005. A continuing saga: the role of testosterone in aggression. *Hormones Behav* 48:253–5.
- Wingfield JC, Hegner RE, Dufty AM, Ball GF. 1990. The “Challenge Hypothesis”: theoretical implications for patterns of testosterone secretion, mating systems, and breeding strategies. *Am Natural* 136:829–46.
- Wingfield JC, Maney DL, Breuner CW, Jacobs JD, Lynn S, Ramenofsky M, Richardson RD. 1998. Ecological bases of hormone-behavior interactions: the “emergency life history stage”. *Am Zool* 38:191–206.
- Wingfield JC, Sapolsky RM. 2003. Reproduction and resistance to stress: when and how. *J Neuroendocrinol* 15:711–24.
- Yanase T, Fan W, Kyoya K, Min L, Takayanagi R, Kato S, Nawata H. 2008. Androgens and metabolic syndrome: Lessons from androgen receptor knock out (ARKO) mice. *J Steroid Biochem Mol Biol* 109:254–7.
- Zuk M. 1996. Disease, endocrine-immune interactions, and sexual selection. *Ecology* 77:1037–42.
- Zuk M, Johnsen T, Maclarty T. 1995. Endocrine-immune interactions, ornaments and mate choice in red jungle fowl. *Proc Roy Soc B* 260:205–10.