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Introduction. Integration of ecology and endocrinology in avian reproduction: a new synthesis

Birds are some of the most familiar organisms of global ecosystems. Changes in the visibility and abundance of birds are therefore excellent indicators of population and physiological responses to habitat changes and are a major focus for public concern about detrimental environmental changes. In order to understand how birds respond to these challenges, it is essential to determine how the environment affects reproduction under natural conditions. The continuum from environmental variables (cues) to reproductive life-history traits depends upon a cascade of neural and physiological processes that determine the extent and rate at which birds will be able to adapt to changes in their environment. For a full understanding of this ability to adapt, ecologists and endocrinologists need to collaborate and build a common framework. The objective of this theme issue is to bring together a series of papers addressing how evolutionary ecologists and endocrinologists can collaborate directly using avian reproduction as a model system. First, we address the need to integrate ecology and endocrinology and what benefits to biological knowledge will be gained. The papers collected in this issue represent a new synthesis of ecology and endocrinology as discussed in three E-BIRD workshops. The three main foci are trade-offs and constraints, maternal effects and individual variation. Authors within each group present ecological and endocrinological aspects of their topics and many go on to outline testable hypotheses. Finally, we discuss where the major problems remain and how this issue points out where these need collaborative efforts of ecologists and endocrinologists. Specific challenges are raised to future researchers to break through intellectual barriers and explore new frontiers. This framework of topics will ultimately apply to all taxa because the principles involved are universal and hopefully will have direct application to programmes integrating organisms and genes throughout biological sciences.

Keywords: ecology; endocrinology; evolution; global warming; climate change; maternal effects

1. INTRODUCTION

Spectacular advances have been made in numerous disciplines of biological sciences that focus either on genes, cells, individuals, populations, ecosystems or their components. Although many research disciplines are developing extremely rapidly in an independent way, the greatest future challenge will be how to integrate all this multi-level knowledge (e.g. Jasanoff *et al.* 1997). Scientific advances in some disciplines are currently severely limited by lack of understanding of mechanisms and processes that have been traditionally considered the purview of other disciplines. For example, evolutionary biologists want to know how biological traits are shaped by natural and sexual selection at evolutionary time scales. They examine how interactions between individual decisions (i.e. phenotypic expression) and environmental selection pressures influence offspring production and survival and their effects on population and ecosystem dynamics. These research fields often ignore the underlying physiological control mechanisms responsible for the developmental processes that result in expression and plasticity of phenotypes (optimal decision rules). Such mechanisms determine to what extent organisms are constrained in their ability to respond optimally to environmental change, and thus also determine the expression of suboptimal decision rules resulting in maladaptive phenotypic expression in novel environments (Ricklefs & Wikelski 2002; Visser *et al.* 2004). Hormones play an essential role in these mechanisms because many are produced in or may act through the central nervous system, and thereby form the stepping stone linking the stimuli from the environment to phenotypic expressions. Hormones also play a major role in regulating responses to environmental perturbations or anthropogenic disturbances, such as global climate change and environmental degradation, that can have profound effects on individual and population survival. At the other extreme, although sequencing of various genomes from yeast to human is greatly expanding our understanding of both the diversity and the conservation of genetic information, how does one proceed from a gene sequence to its physiological or biological role? Linking genes to specific actions is a considerable problem largely because genes work via complex biological pathways and not in isolation (Cohen 1997; Pfaff 1997). The particular functions of a differentiated cell involve a complex interaction of many proteins that can be modified by hormones. Coordination of gene activity among various cells and tissues of the organism culminating in response to internal or external environmental signals also involves hormones.

Researchers who focus on the proximate mechanisms are aware that physiological control mechanisms can be studied in a demographic and evolutionary context,

One contribution of 12 to a Theme Issue 'Integration of ecology and endocrinology in avian reproduction: a new synthesis'.

but often they do not take fitness, population and ecosystem consequences of their mechanisms into account. Although widely advocated, the evolutionary viewpoint of ecology and the mechanistic viewpoint of physiology/endocrinology are rarely examined in a single study. There is however a growing interest in combining these different viewpoints (e.g. Ketterson & Nolan 1999; Feder *et al.* 2000; Zera & Harshman 2001; Zera *et al.* 2007), and multidisciplinary studies and approaches are needed. Integrated, multidisciplinary fundamental research at different biological scales becomes indispensable given that selection shapes physiological control mechanisms across generations, and that developmental processes determine optimal responses to selection processes within generations. Many biologists understand that we will require integrated interdisciplinary work at both the biological and the methodological levels to make significant fundamental scientific progress. This progress should be expressed in the identification of processes involved in the transition between different biological scales of organization, and more specifically, to improve our understanding of why and how components of organisms, the organisms themselves and the populations and ecosystems to which they belong interact and cope with global environmental change.

2. E-BIRD NETWORK: INTEGRATING ECOLOGY AND PHYSIOLOGY

Given the central importance of integrating environmental endocrinology and evolutionary ecology, a research coordination network was formed and focused on the integration of endocrinology and ecology of birds. The network served to bring together investigators with the collective expertise to achieve this integration. While ecologists and endocrinologists do not have a history of working together to solve problems in basic or applied science, members of both disciplines are trained to think in terms of multivariate, systems-level interactions as well as positive and negative feedback in regulatory control. Birds are highly visible components of the world's ecosystems, and changes in their visibility and abundance are a major focus for public concern about, and scientific interest in, possible detrimental environmental changes (Walther *et al.* 2002). Currently, bird populations are affected by large-scale climate change and changes in land use associated both with climate change and due to increasing demands from agriculture, forestry and urban development. Owing to the availability of long-term phenological datasets, bird studies have, for example, provided some of the best evidence to date for impacts of climate change (Parmesan & Yohe 2003; Visser & Both 2005). In order to understand how birds can cope with these threats, we need to determine how the environment and its variations influence one of the most extensively investigated aspects in biological sciences: reproduction. The transition from environmental cues to reproductive traits depends upon a cascade of neural and physiological processes including perception of the environment, and translation of environmental information into neuroendocrine and endocrine secretions that then regulate reproductive function and expression. The underlying mechanisms of these biological-scale transitions determine the extent and rate at which birds adjust reproductive decisions to habitat modifications. Fully understanding these processes at the individual level and its demographic and evolutionary consequences for population functioning requires collaboration networks to foster the necessary exchange of knowledge and expertise between researchers with distinct scientific backgrounds.

In 2002, a workshop entitled 'Adaptation and constraints in avian reproduction: integrating ecology and endocrinology' was organized to bring together specialists working on avian reproduction. The aim was to establish contacts and initiate discussions of how ecologists and endocrinologists can collaborate in future research networks. A common goal was to ameliorate simultaneously the knowledge of the proximate and ultimate determinants of reproductive traits in free-living bird populations that face rapid environmental change. As bird population changes are global rather than local issues, scientists from Europe, USA and Canada were invited to join the workshop. This initial workshop led to the establishment of the international E-BIRD network, financed by the European Science Foundation, the National Science Foundation (USA) and the Natural Sciences and Engineering Research Council (Canada).

This theme issue is the outcome of activities from the three focused E-BIRD workshops (trade-offs and constraints, maternal effects and individual variation), co-organized by North-American and European researchers. For each of the workshop activities, we present integrated visions of researchers with a range of scientific backgrounds from evolutionary ecology to physiology to underline potential differences in opinion and approaches, as well as examples of successful integrated research. We hope that this E-BIRD special issue of *Philosophical Transactions of the Royal Society B* will provide stimulating examples for all investigators of complex global ecological problems, whatever be the biological model systems involved. We also hope that the papers in this issue will have an impact on education at undergraduate and graduate levels and will facilitate a truly integrative biology curriculum including conservation biology.

The theme is organized along the lines of the workshops in three major topics. First, 'trade-offs and constraints', second, 'maternal effects' and third, 'individual variation'. Within each topic, papers consider ecological, physiological and integrative aspects. Here, we also comment on the key issues that arose in each section and what future research should address.

(a) *Trade-offs and constraints*

Historically, ecologists and endocrinologists have taken very different approaches to understanding avian life histories. While endocrinologists have been involved in unravelling the complexities of the physiological causal mechanisms, ecologists have focused on understanding the selection pressures that have led to the evolution of the life histories that we now observe. This separation of the two research traditions is exemplified in ecologists' use of what has been referred to as the 'phenotypic gambit': assuming that physiological (and genetic) control mechanisms do not constrain the outcome of evolution. This approach has yielded many useful insights, but it is now becoming clear that further progress will be hampered if ecologists continue to ignore physiological mechanisms.

The incorporation of physiological mechanisms into evolutionary ecology is especially important for life-history traits. These trait values are not only fixed by the genotype of the individual but are also influenced by its environment. Evolutionary ecologists study this so-called phenotypic plasticity (described by a reaction norm: the curve describing how the phenotype is affected by the environment) by estimating trade-offs, such as between current and future reproductive success, and by constraints, such as the maximal daily energy expenditure. Using this knowledge, they calculate the optimal phenotypes for the different environments and compare this to the observed reaction norm. The question is to what extent the differences between optimal and observed plasticity can be understood from the underlying hormonal control mechanisms.

The further integration of causal mechanisms and evolutionary models is especially important when we need to extrapolate reaction norms outside the natural range, for instance to understand how species will respond to large-scale changes, such as climate change. Furthermore, under such novel environmental conditions, the mechanism may no longer lead to adaptive phenotypic plasticity, which will lead to consistent directional selection on the mechanism underlying this plasticity. To understand the rate at which plasticity will respond to this selection, we need to understand the mechanism, including for instance the way traits are correlated via the hormonal control system.

In the section on trade-offs and constraints of this special issue, there are four contributions that address the question how hormonal control mechanisms affect the outcome of selection on life-history traits.

In the contribution of Lessells (2008), the central question is to what extent phenotypic plasticity is shaped by the underlying mechanism. In which cases do evolutionary ecologists need to take the details of the neuroendocrine control mechanism that underlies the reaction norm into account? Lessells argues that this is important in two cases: the first is when the neuroendocrine system may not be able to provide the optimal solution. For instance, in extremely warm springs, it may be optimal to lay eggs very early in the season but when initial gonadal development is triggered by photoperiod, the system may simply not be ready and hence constrains the reaction norm of laying date versus temperature. Since this will especially play a role in changing environments, as under the condition under which a species has evolved, we would expect natural selection on the mechanism to have solved this problem. The second way in which the characteristics of the mechanism may shape phenotypic plasticity is when there are costs of the neuroendocrine system. Lessells carefully discusses which of these, such as the costs of hormone synthesis or toxicity of hormones, would matter. These insights will be stimulating to endocrinologists to rethink their views on the costs of, for instance, elevated testosterone levels in aggressive encounters.

Dawson (2008) discusses the interplay between the ecological conditions that determine optimal seasonal time of reproduction, moult, etc., and the underlying endocrine mechanisms. He emphasizes that under different environmental conditions different mechanisms that underlie phenotypic plasticity in reproductive timing will be selected for. The key point is the degree of predictability of the annual fluctuation in environmental conditions. While the response to photoperiod plays an essential role in the seasonal timing of almost all species (opportunistic breeders are the exception), the additional (or supplementary) cues used by a species strongly depend on the species' ecology. Understanding these mechanisms underlying phenotypic plasticity is essential when predicting how species will respond to environmental change.

In their contribution, McGlothlin & Ketterson (2008) focus on correlated traits that are often mediated by hormones and the authors evaluate such hormone-mediated suites of traits using a quantitative genetic framework. Correlations between traits can be the outcome of natural selection but, especially in a changing environment, can also constrain the rate of microevolution. In new environments a different correlation between trait values is optimal and hence natural selection will act on these correlations. Their contribution highlights the importance of combining in depth endocrine studies with quantitative genetics in an ecological setting. Only then, as they put it, we will 'understand how the inside world of organisms becomes adapted to the outside world'.

The contribution of Adkins-Regan (2008) questions whether or not the hormonal control system is likely to constrain the rate of evolution, and she explores this by looking in detail at three systems: the hypothalamic–pituitary–gonadal (HPG) axis; effect of sex steroids on mating behaviour; and sexual differentiation. Only for the last case does she conclude that the hormonal control system may contribute to evolutionary inertia. But, in the case of the HPG axis, Adkins-Regan argues that there is considerable plasticity in the system and also that it is probably ancient having survived many large-scale environmental changes. Adkins-Regan thus has an optimistic view on the degree of constraint on the system, perhaps due to her more comparative, across species, approach for which the time scale over which evolution takes place is much longer than the time scale of microevolution (focusing on within-species rates of adaptation).

(b) *Maternal effects*

One of the most important recent developments in the studies of the evolution of life histories is the recognition that state of the parent during offspring production has a profound and permanent effect on offspring morphology, physiology and behaviour. Particularly surprising has been the discovery that parents can tailor the phenotype of their offspring to suit prevailing environmental conditions; offspring sex, growth rate and competitive behaviour can be altered in response to changes in environmental factors such as food availability, predation risk, social density and the level of competition. However, we know very little about the mechanisms and constraints that underlie such effects, the costs and benefits involved or the time scales over which different effects operate. This is important since rapid environmental change may disrupt a delicately balanced interplay between organism and environment. Birds are particularly useful in such studies because the avian egg is a sealed system: the female is able to put a complex cocktail of substances into the egg that influences the developing embryo, and this system is easily accessible for study of maternal effects. Maternal hormones have been shown to be of great importance here.

The first paper by Monaghan (2008) leads off with the statement 'the environment is not merely "permissive" of development, but to some extent also guides, or even induces it' (see also Gilbert 2005). This immediately raises questions of how responses to environmental cues, mediated through maternal effects, evolved *and* what the mechanisms by which they are manifested might be (a classical role for hormones). She goes on to outline what information is needed from researchers to understand how the phenotype is tailored by development and the adult environment. This interaction is also particularly vulnerable to global climate change. Monaghan then presents some simple models of the interactions of adult environment and developmental conditions the phenotype experienced. For example, individuals born under good environmental conditions for the adult will have the greatest fitness under good adult conditions in the future and higher fitness than individuals that developed under poor conditions. Individuals that developed under poor environmental conditions will also benefit from good conditions as an adult, but will tend to have higher fitness if adult conditions become poor. These models are an excellent framework for future research at evolutionary levels as well as for mechanisms.

The second paper by Groothuis & Schwabl (2008) is an excellent, critical and in-depth analysis of what we know about hormone mechanisms of maternal effects. The focus is on egg yolk as a source of maternal hormones that may direct development at least early on in ontogeny, i.e. before the embryo beings to produce its own hormones. This is a rapidly expanding field and this review is timely. The authors have three major foci. First, how do hormones get into the yolk and to what extent do females have control over the amount that each egg ultimately accumulates? Second, for the hormones in yolk to be effective, there must be metabolizing enzymes and receptors for those hormones at a very early stage. By the time the embryo begins forming its own hormones, they tend to be present at higher concentrations than in yolk; therefore, the mechanisms of action very early in ontogeny are critical. Third, the pathways by which maternal hormones in yolk influence the final phenotype that develops are largely unknown. Key issues raised by Groothuis & Schwabl and the models presented by Monaghan provide us with a very useful framework to begin exploring this aspect of developmental biology.

The third paper in this group by Martin & Schwabl (2008) is a natural sequel to the first two because it actually takes real datasets from 83 species of birds in the tropics and temperate zones. The authors compare development rates and parental investment in relation to longevity, predation risk and energetics (costs) to show that females not only use proximate pathways to adjust incubation periods and offspring quality but also maternal strategies are subject to strong selection from adult and offspring mortality. This analysis then sets up endocrinological studies on variation in androgen deposition into yolk that has been shown to influence development rates of embryos. The comparison of tropical and temperate zone species with different rates of development and maternal attentiveness is a clear example of how ecologists and endocrinologists can interact. Much more work is needed to resolve the mechanisms but these papers provide a clear pathway for the future.

The fourth paper of this group is by Rutkowska & Badyaev (2008) and addresses a long-standing problem of how sex ratio of offspring may be modulated. We know that for many vertebrates such as some reptiles, amphibians and fishes, sex is determined by environmental conditions during development. However, for other species, and as far as we know all birds and mammals, sex is genetically determined but, nonetheless, many ecological studies have shown that the sex ratio can be manipulated. This can occur by several potential mechanisms. For example, both maternal and paternal effects can determine which sex survives to hatching/birth and which sex reaches maturity (secondary and tertiary sex ratios). But one major problem remains as to how females may influence which ovum, male or female, actually is laid or implants in the uterus. This regulation of the primary sex ratio is the focus of Rutkowska & Badyaev. They point out that ecological studies show that despite genetic sex, primary sex ratio is manipulated and they discuss the evolution of biasing towards males or females. They then review molecular and cytological mechanisms of meiosis in birds and point out that many mechanisms may exist by which females could bias sex ratio in a clutch of eggs. Birds are ideal subjects because females are the heterogametic sex. Hormones may also be involved. This contribution goes beyond review and suggests ways in which this fascinating and fundamental problem might be approached. It is a challenge to us all to truly integrate ecology and evolution with endocrinology, molecular and cell biology.

(c) *Individual variation*

As the contribution of Lessells highlights, a recurring theme (see above) of the E-BIRD workshops has been that evolutionary ecologists and endocrinologists have traditionally taken fundamentally different approaches to the same general biological problems. Evolutionary ecologists have attempted to understand how selection pressures favour one particular phenotype, or life history, over another and thus how phenotypes change or evolve in response to selection. Endocrinologists on the other hand have focused on the mechanisms that underlie 'the chain of causation from the perception of the environment, via the workings of the neuroendocrine system, to the production of a particular morphological, physiological or behavioural phenotype' (Lessells 2008). As mentioned above, evolutionary ecologists have tended to embrace individual (phenotypic) variation since heritable variation within populations is the raw material on which natural selection acts and without which evolution cannot occur. Individual-based models and approaches are now widely used in subdisciplines such as behavioural ecology, population biology and evolutionary biology (e.g. Bolnick *et al.* 2003; Breckling *et al.* 2006; Reale *et al.* 2007). In contrast, endocrinologists (indeed physiologists in general; Bennett 1987) have largely ignored individual variation, driven in part by a 'desire to discover general processes or identify central mechanisms' (Ball & Balthazart 2008).

The third E-BIRD workshop on individual variation sought to determine how to make progress towards solving the key questions that an individual-based approach would ask with respect to *ecological* endocrinology: (i) to what extent does variation in physiological measures across individuals represent short-term variation (sampling error) and to what extent are there repeatable differences across individuals, suggesting the existence of 'physiological phenotypes'; (ii) can differences in physiological measures across individuals be explained by processes occurring over short-term and longer-term time scales; for example, how much variation is due to behavioural plasticity and how much is due to environmental-, parental- or origin-specific effects; (iii) how much of the within-individual variation reflects differences in the specific state of control mechanisms and how much to differences in control mechanisms between individuals; (iv) can we study variation in the physiological control mechanisms that influence ecologically important traits in ecologically realistic conditions; and (v) how do we design experiments to incorporate individual variation, e.g. how important are 'baseline', pre-treatment measurements and repeated measures designs versus cross-sectional designs (indeed is there such a thing as a true physiological or endocrinological baseline)?

An individual-based approach to *ecological* endocrinology will probably require new ways of thinking about, analysing and interpreting variability and methodological issues. For example, many studies report highly significant relationships between two variables based on regression analysis, but where the explanatory variable (x) only explains approximately 10% of the variation in the dependent variable (y). In cases like this, should we be satisfied with the statistically significant regression or should we focus more on explaining the huge variability in the y-variable for any particular value of the x-variable (i.e. what explains the 'other' 90% of the variation)? As a further example, many 'adaptive' hypotheses for hormone variation imply that relatively small differences in *average* hormone level (5–10%) can have significant effects on phenotypic trait values, but fail to explain why even greater inter-individual variation (100%) does not have even larger, overriding effects on phenotype. Three contributions from the 'individual variation' workshop in this special issue address what we know, and what we need to know, about inter-individual variation in endocrine systems.

Williams (2008) focuses on variation in hormone titres (i.e. plasma hormone levels) to argue that comparative endocrinologists largely ignore inter-individual variability. This paper highlights both the challenges and the opportunities of a renewed focus on inter-individual variation in endocrine systems, particularly in the context of life histories and evolutionary responses to environmental change. The challenges are to 'conventional wisdom' in endocrinology itself, e.g. re-evaluation of relatively simple, but unresolved questions such as structure–function relationships among hormone, binding globulins and receptors, and the functional significance of absolute versus relative hormone titres. Opportunities include endocrinologists contributing solid mechanistic understanding to key questions in evolutionary biology, e.g. *how* endocrine regulation is involved in evolution of complex suites of traits or how hormone pleiotropy regulates trade-offs among life-history traits. Williams also stresses the value of endocrinologists adopting conceptual and analytical approaches already widely used in evolutionary biology for the quantitative analysis of inter-individual variation (e.g. selection studies, reaction norms, concepts of evolutionary design, etc.).

In a complementary paper, Ball & Balthazart (2008) review what is known about individual variation and the endocrine regulation of behaviour in birds from a cellular and molecular perspective. They provide a detailed review of 'what ecologists and anyone considering integrative approaches' need to know about the complexities of endocrine signalling including hormone-binding globulins, intracellular signalling, and receptor and co-regulator function, and they provide examples where consideration of cellular/molecular variables related to the effectiveness of steroid hormones have been useful in understanding the regulation of individual behaviour. Ball & Balthazart suggest that one strategy for investigating inter-individual variation in endocrine systems is to learn from studies of large units of intraspecific variation, such as population or sex differences, to provide ideas about variables that might be important in explaining continuous individual variation. They conclude that this approach along with the use of newly developed molecular genetics tools represents a promising avenue for avian ecophysiologists to pursue.

The paper by Kempenaers *et al.* (2008) provides a detailed empirical example of both the magnitude and the patterns of inter-individual variation in plasma testosterone levels in a well-studied, free-living passerine, the blue tit (*Cyanistes caeruleus*), in ecologically realistic conditions. They highlight the fact that the sources and the implications of the large variability in individual testosterone levels within the seasonal cycle surprisingly are not well understood, but that such an understanding is critically important for behavioural and evolutionary ecologists (e.g. in relation to testosterone's role in 'honest sexual signalling' theory, as a hypothesized key mediator of life-history trade-offs). Kempenaers *et al.* discuss whether individual variability mainly reflects differences in the underlying individual quality (intrinsic factors such as genetic or maternal effects) or in the environment (extrinsic factors including time of day, individual territorial status and past experience). They conclude that research in avian behavioural endocrinology has mainly focused on the effects of extrinsic factors, while other sources of variance are often ignored, and suggest that studies that use an integrative approach to investigate the relative importance of all potential sources of variation are essential for correct interpretation of data on individual variation in plasma hormone levels.

3. DIFFERENT VIEWPOINTS AND CONVERGING VIEWPOINTS

Although we believe that E-BIRD has been very successful in encouraging and facilitating dialogue, integration and future collaboration between evolutionary ecologists and endocrinologists, it is clear from the papers included in this special issue that significantly different viewpoints remain (among endocrinologists and among ecologists) even as converging viewpoints emerge. Here, we highlight some of these contrasts and commonalities with a view to identifying key questions and challenges for future research in this area.

Many comparative and field endocrinologists continue to measure hormone titres, i.e. *plasma* hormone levels. This approach has proved very useful over longer time scales such as seasons. For example, most, if not all, individuals show marked changes in gonadotrophins and sex steroids during puberty or seasonal expression of reproduction. But at any point in development of the reproductive system (and its regression), considerable individual variation remains unexplained. What is the functional significance of the marked inter-individual variation in hormone titres? Ball & Balthazart (2008) state that although variation in hormone titres or plasma levels *might* explain individual variation in behaviour and physiology, such attempts 'have generally failed' at least with regard to behaviour (see also Adkins-Regan 2008). In contrast, Williams argues that selection studies not only provide evidence for the functional significance of hormone titres from correlated responses of hormone-dependent traits, but that these studies also suggest that changes in hormone titres can drive evolutionary changes in other cellular and molecular components of endocrine systems (e.g. receptors). Here, a key unresolved issue is the extent to which sex and gender differences—which are often used to investigate the functional significance of hormone titres—are based on the same mechanisms as individual differences in continuously distributed phenotypic traits. Are there fundamental differences in mechanisms of individual variation for behavioural versus physiological traits? If, as Ball & Balthazart suggest, plasma hormone levels are usually much higher than the minimum required for behavioural activation, what is the reason for this 'excess capacity' (Williams 2008), particularly in the context of potential costs of endocrine systems acting as constraints (Lessells 2008). Similar questions arise when considering other components of the endocrine system: Ball & Balthazart suggest that hormone-binding globulins could play a regulatory role in fine-tuning endocrine mechanisms to individual variation, whereas Williams stresses the disparity between binding-globulin levels and functional requirements and suggests that this highlights some major unresolved issues with regard to the evolution of binding-globulin function. It is known that corticosteroid-binding globulin can be modulated over a period of hours and that this can have a profound effect on the free concentration of glucocorticoid in blood that can presumably then enter cells, and the extent to which genomic receptors are occupied (Lynn *et al.* 2004). More studies of this kind might help resolve some of these questions.

Section 2*b* also raises many unresolved questions. One obvious question is our need to explore mechanisms that might underlie potential adaptive adjustments of offspring phenotype via hormone-mediated processes (Groothuis & Schwabl 2008) and adaptive adjustments of sex ratio. Assumptions have been made of adaptive strategies, but our knowledge of underlying mechanisms has lagged far behind. For example, effects of maternal steroids in yolk probably are most effective during embryonic development before the embryo begins producing it own hormones. For this to be true, there must be some form of receptor for the hormone if it is to have any biological effect. This fundamental mechanism remains unknown. Rutkowska & Badyaev (2008) indicate the complexity of potential control mechanisms with regard to sex ratio, which not only highlights the scale, but also the opportunity, of this challenge.

Another major unresolved question is the extent to which hormones cause trade-offs among life-history traits, or whether they simply mediate (i.e. provide the mechanism for) trade-offs that result from allocation decisions over limited energy/nutrients reserves. Reed *et al.* (2006) point out our lack of knowledge of 'costs', both direct and indirect (see also Lessells 2008), associated with different components of the endocrine system and review a long-term study of dark-eyed juncos, *Junco hyemalis*, as an example of what can be achieved. Hau (2007) provides an eminently testable set of hypotheses concerning potential trade-offs in the action of testosterone in males. She also points out that there is emerging evidence that mechanisms by which testosterone acts may be more diverse than we thought.

The E-BIRD network and this special issue have focused on building a common framework for endocrinological and ecological research. One aspect that has only been touched upon in passing is that not only terminology and research focus differ but also the type of experiments. While, for instance, endocrinologists frequently focus on males, ecologists tend to study females, and while timing of reproduction by endocrinologists is measured by hormones and gonadal sizes, ecologists look at laying dates (see also Dawson 2008). Joint experiments are needed in which all these parameters are measured to determine the relationship between, for instance, the rate of gonadal growth and laying date.

The integration of endocrinology and ecology is essential to make progress. However, it is just a first step. Especially, if we want to understand the rate at which animals will be able to adapt to large-scale environmental changes, we will need to assess the rate of microevolution, and hence also integrate quantitative genetics in a common framework. While much is known about quantitative genetics of life-history traits, such as laying dates, we need to be aware that any genetic variation on which selection can act is genetic variation in the underlying mechanism. Thus, the challenge is not only to understand this mechanism underlying life-history traits but also to identify the genetic variation in the components of the mechanism. For instance, heritability of timing of reproduction may be due to heritable variation in sensitivity to photoperiod or to temperature. Hence, endocrinologists may start looking for variation in hormone titres, etc. and when data on relatives are available, they start estimating heritabilities. The section on individual variation of this special issue is a start to do so.

Overall, we feel that this series of papers not only summarizes the workshops organized by the E-BIRD network, but it also points the way for the future with clear problems to address for both ecologists and endocrinologists. The special issue indicates how researchers in these two distinct disciplines can work together to solve common problems and provide major conceptual advances in environmental biology in general. This is timely since the effects of global warming and human disturbance are increasing, and we need to know whether organisms may cope—or not.

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