Integrative and Comparative Biology
Integrative and Comparative Biology, volume 62, number 4, pp. 958–971
https://doi.org/10.1093/icb/icac121
Society for Integrative and Comparative Biology

SYMPOSIUM INTRODUCTION

Vertebrate Phenological Plasticity: From Molecular Mechanisms to Ecological and Evolutionary Implications

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From the symposium “Phenological plasticity: from molecular mechanisms to ecological and evolutionary implications” presented at the annual meeting of the Society for Integrative and Comparative Biology virtual annual meeting, January 3–February 28, 2022.

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Synopsis Seasonal variation in the availability of essential resources is one of the most important drivers of natural selection on the phasing and duration of annually recurring life-cycle events. Shifts in seasonal timing are among the most commonly reported responses to climate change and the capacity of organisms to adjust their timing, either through phenotypic plasticity or evolution, is a critical component of resilience. Despite growing interest in documenting and forecasting the impacts of climate change on phenology, our ability to predict how individuals, populations, and species might alter their seasonal timing in response to their changing environments is constrained by limited knowledge regarding the cues animals use to adjust timing, the endogenous genetic and molecular mechanisms that transduce cues into neural and endocrine signals, and the inherent capacity of animals to alter their timing and phasing within annual cycles. Further, the fitness consequences of phenological responses are often due to biotic interactions within and across trophic levels, rather than being simple outcomes of responses to changes in the abiotic environment. Here, we review the current state of knowledge regarding the mechanisms that control seasonal timing in vertebrates, as well as the ecological and evolutionary consequences of individual, population, and species-level variation in phenological responsiveness. Understanding the causes and consequences of climate-driven phenological shifts requires combining ecological, evolutionary, and mechanistic approaches at individual, populational, and community scales. Thus, to make progress in forecasting phenological responses and demographic consequences, we need to further develop interdisciplinary networks focused on climate change science.

Introduction

Seasonal timing or “phenology” of biological events is being altered in many plants and animals in response to climate change (Parmesan 2006; Renner and Zohner 2018). In some species, however, changes in phenology have not been evident or have been insufficient to track rapid changes in their environment, leading to desynchrony between interacting species (Stenseth and Mysterud 2002; Post and Forchhammer 2007). For example, disrupted synchrony between life history timing of consumers and the phenology of the resources on which they rely has been linked to widespread population declines (Both et al. 2006; Møller et al. 2008; Iler et al. 2021), and even to effects on ecosystem function (Beard et al. 2019). Given ongoing warming and changes in patterns of precipitation, it is becoming increasingly clear that the capacity of organisms to appropriately adjust their phenology, either through phenotypic plasticity or microevolution, is a critical component of resilience.

Despite general interest in predicting how individual species will adjust their seasonal timing in response to climate change, our ability to do so is constrained

Advance Access publication July 22, 2022

by limited knowledge regarding the cues used to adjust timing and the endogenous genetic and molecular mechanisms that transduce cues into neural and endocrine signals. Further, while there is widespread agreement that climate change is leading to phenological mismatches, determining the impacts of a changing climate on pair-wise species interactions, communities, and ecosystems remains a formidable task and our ability to discriminate between systems where these mismatches are likely is currently limited (Kharouba and Wolkovich 2020).

More than a decade ago, Visser et al. (2010) proposed that the integration of a more interdisciplinary framework was needed to develop better forecasts for climate change impacts on phenology. In the intervening years, significant advances have occurred across biological levels of organization, indicating promise towards the development of better approaches for predicting phenological responses and their consequences. For example, molecular biologists have recently made significant strides in elucidating the neuroendocrine mechanisms that govern seasonal and circannual rhythms (Wood and Loudon 2014; Dardente et al. 2019); physiologists have made progress in identifying how the links between sensory circuits and control mechanisms allow individuals to modulate seasonal timing in response to external environmental cues and endogenous state (Williams et al. 2017; Chmura et al. 2019; van Rosmalen et al. 2021); population ecologists have been able to quantify the impact of phenological shifts on individual fitness and population dynamics (Lane et al. 2012; Kingsolver and Buckley 2018); and evolutionary biologists are taking advantages of new molecular tools to document evolutionary changes in phenological traits across generations (Saino et al. 2017; Visser and Gienapp 2019). Nevertheless, significant challenges remain, and our ability to predict how species will respond to climate change remains unreliable (Renner and Zohner 2018). Further, while it is widely recognized that asynchronous phenological shifts between interacting species may have broad ecosystem-level consequences, our mechanistic understanding of the processes involved is insufficient to apply findings across sites or systems (Kharouba and Wolkovich 2020).

In this symposium and issue of Integrative and Comparative Biology, we bring together molecular, physiological, ecological, and evolutionary perspectives to stimulate cross-disciplinary dialogue and promote greater inter-disciplinary collaboration. Our primary goal is to build on the integrative approaches advocated by Visser et al. (2010) and to work towards a more holistic understanding of phenological plasticity that spans hierarchical levels, from the sensory circuits and neuroendocrine control systems that allow individuals to alter their seasonal timing to the population and community-level responses that characterize ecological and evolutionary ramifications. As part of our efforts to connect transdisciplinary dots, we provide a brief overview on the current state of knowledge regarding molecular, ecological, and evolutionary aspects of vertebrate phenological responses to climate change.

Molecular control mechanisms

Ultimately, many vertebrates maximize their fitness and reproduction by timing energetically expensive, annually recurring, life-history events (e.g., reproduction) to coincide with high levels of resource availability. However, on a proximate level, seasonal timing is dictated by the perception, integration, and transduction of reliable environmental cues that allow an animal to anticipate predictable changes in resource availability (Ball and Ketterson 2008; Caro et al. 2013; Wingfield 2015). In vertebrates, these cues are integrated, in part, by endogenous clock mechanisms (i.e., circadian and circannual clocks) that allow animals to synchronize their biology with the external environment. For most vertebrates, photoperiod is an exceptionally reliable cue and is critical in triggering seasonal physiological changes. However, climate change has no impact on seasonal cycles of photoperiodic change, and thus animals are reliant on secondary cues to plastically adjust their timing to maintain synchrony with the changing environment (Fig. 1). As such, it is critical to understand how taxonomic variation in the cues animals use to time their seasonal physiology and behavior leads to variability in phenological responses.

The photoperiodic response

In non-equatorial regions, a changing photoperiod is the most reliable cue of seasonality and the photoperiodic response, which involves detecting and translating changes in daylength into neuroendocrine signals, is critical to fitness in most organisms (Nakane and Yoshimura 2019). Many aspects of the photoperiodic neuroendocrine axis are conserved across vertebrates (O'Brien et al. 2012), although some notable differences are present and more work is needed to determine how much these pathways have diverged (Maugars et al. 2014; Lorgen et al. 2015).

The photoperiodic response requires light receptors that transmit light–dark information to circadian oscillators that act to "measure" daylength and activate neuroendocrine pathways that orchestrate seasonal changes in physiology and behavior (Nakane and Yoshimura 2019) (Fig. 2). In mammals, light received by rods and cones is transmitted to intrinsically photosensitive retinal ganglion cells (ipRGCs), which also receive light

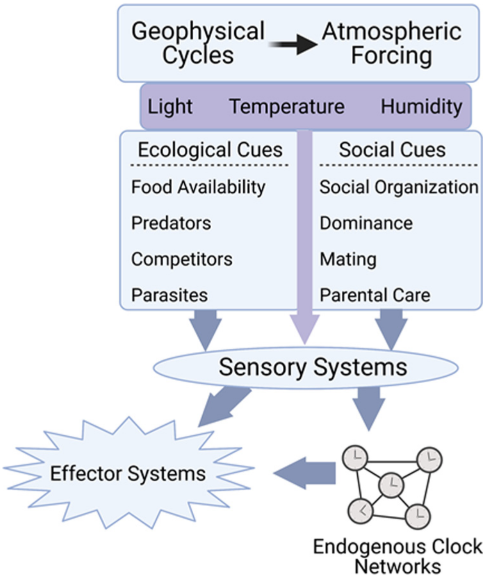

Fig. 1 Geophysical cycles and atmospheric forcing drive changes in the abiotic environment (e.g., light, temperature, and humidity) which, in turn, affect ecosystem function. Abiotic cues, in combination with social and ecological cues are perceived by sensory systems which alter effector systems and timing directly, or indirectly via endogenous clock networks.

using the pigment melanopsin (Lucas et al. 2014). These ipRGCs then transmit this information via the retinohypothalamic tract to the suprachiasmatic nucleus (SCN) of the hypothalamus, which acts as a "master" circadian clock (Reppert and Weaver 2002). The SCN drives the rhythmic release of melatonin from the pineal gland, which acts as an internal signal of photoperiod (Goldman and Nelson 2020). The pars tuberalis (PT) of the pituitary is one of the primary targets for melatonin (Von Gall et al. 2005; Dardente 2012)—increasing daylength in spring shortens the daily duration of the melatonin signal which is purported to alter the expression of a circadian clock-regulated transcription regulator, EYA3 (Dardente et al. 2010; Masumoto et al. 2010). EYA3, in turn, drives the expression of the TSHβ subunit, leading to a sustained increase in TSH expression in the PT (Wood and Loudon 2014). The increase in TSH alters the expression of deiodinase enzymes (DIO2 and DIO3) in hypothalamic β-tanycytes lining the third ventricle—these cells have basal processes that project into the PT (Rodríguez et al. 2019). Under long days, DIO2 is expressed and converts metabolically inactive thyroxine (T4) to tri-iodothyronine (T3), the most biologically active form of thyroid hormone; in contrast, DIO3, which inactivates thyroid hormone by converting T4 into reverse T3 (rT3) and T3 into diiodothyronine (T2), is expressed under short days with a long melatonin signal (Wood and Loudon 2014). The availability of T3 in the hypothalamus, controlled by this retrograde signaling pathway, appears to be critical in driving seasonal physiological and behavioral changes (Barrett et al. 2007; Ebling and Lewis 2018).

Although the retrograde TH signaling pathway is largely conserved across vertebrates (Hazlerigg and Loudon 2008; Nishiwaki-Ohkawa and Yoshimura 2016), there are significant differences in how photoperiodic cues are transmitted to the PT. In addition to retinal photoreceptors, most non-mammalian vertebrates also perceive light using the pineal (or parapineal organ) and deep brain photoreceptors (Kawano-Yamashita et al. 2014; Pérez et al. 2019). Further, rather than having a masterclock network in the SCN that acts as to entrain peripheral and central circadian clocks (Buhr and Van Gelder 2014), non-mammalian vertebrates possess three major interacting clock networks in the retina, hypothalamus (or brain), and pineal whose relative contribution to rhythmicity appears to vary by species and possibly across time (Gwinner and Brandstatter 2001). Further, many vertebrates are not reliant on melatonin as a cue for daylength and it may only be of significant importance to seasonal timing in mammals (Sáenz de Miera et al. 2018; Nakane and Yoshimura 2019). In non-mammalian vertebrates, it is thought that deep brain photoreception alone can orchestrate seasonal activation of the retrograde thyroid hormone signaling pathway (Pérez et al. 2019). Though the mechanisms through which this occurs remain uncertain, Opsin-5 neurons in the paraventricular organ may regulate seasonal reproduction, at least in birds (Nakane et al. 2010). Finally, fish lack an anatomically distinct PT and instead a region called the saccus vasculosus appears to be used to transduce photoperiodic cues into a neuroendocrine signal (Nakane et al. 2013).

To date, most research has focused on the role of hypothalamic T3 in activating or deactivating the reproductive axis, with T3 having stimulatory effects on the reproductive axis of long-day breeders and inhibitory effects in short-day breeders (Sáenz de Miera et al. 2013; Dardente et al. 2019). The cellular and molecular targets of T3 within the mediobasal hypothalamus are unknown, although two RF-amide neurons (kisspeptin and RF-amide related peptide 3 [RFRP-3]; the mammalian ortholog of gonadotropin inhibiting hormone [GnIH]) are proposed as relays between T3 and the gonadotropin-releasing hypothalamus-pituitary-gonadal axis (Dardente et al. 2019).

Although the role of the retrograde T3 signaling pathway on seasonal cycles of reproduction and body mass change is evident, the importance of this pathway for other seasonal cycles is less clear. For example, micro-implantation of T3 within the hypothalamus of long-day breeding hamsters prevents testicular regression and seasonal weight loss when exposed to a

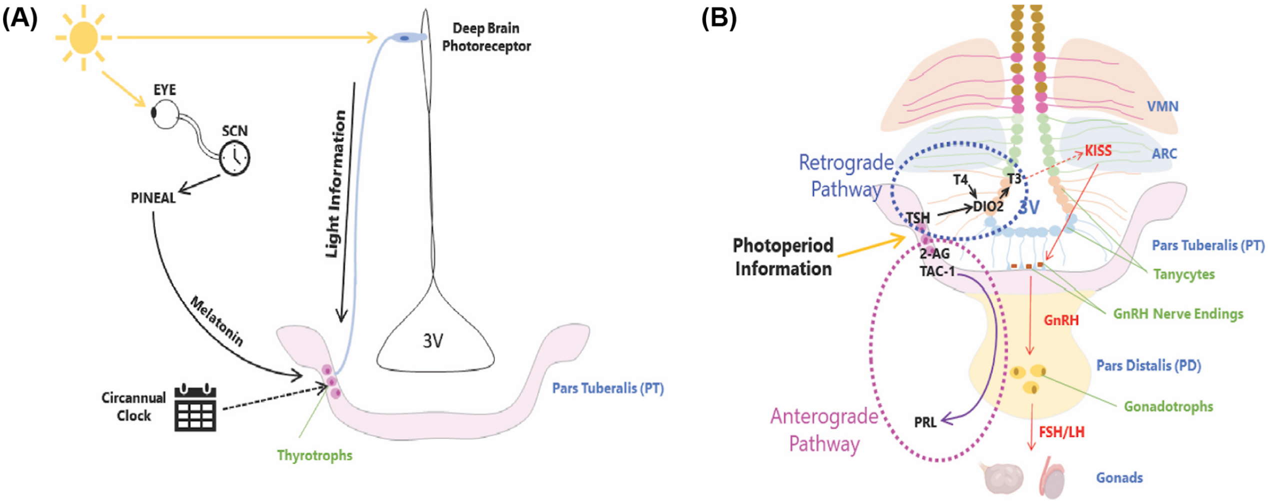

Fig. 2 **(A)** Photoperiodic signal transduction pathways in mammals and birds. In mammals, light is detected by intrinsically photosensitive retinal ganglion cells (ipRGCs) in the eye which transmit the signal to the master circadian clock in the suprachiasmatic nucleus (SCN) of the hypothalamus. Directed by the SCN, the pineal gland secretes the hormone melatonin during the dark phase of the daily cycle, which acts on the pars tuberalis (PT). In birds, the pineal is directly photosensitive and changes in melatonin are not necessary to transduce photoperiodic signals. This is because, in birds, light information is received by deep brain photoreceptors that act directly on the PT. Additionally, some birds and mammals possess innate long-term timers or "circannual clocks," which are hypothesized to be located within the PT. **(B)** Photoperiodic (or circannual) signals trigger the hypertrophy of thyrotroph cells and retrograde action (blue dashed oval) of thyroid stimulating hormone (TSH) on ependymal tanycytes that have cell bodies lining the third ventricle (3V) with processes extending to PT. The increase in TSH expression alters the expression of deiodinase enzymes (DIOs) within the tanycyte cells—increased DIO2 expression and decreased DIO3 expression (not shown) results in localized increases in triiodothyronine (T3), the most biologically active form of thyroid hormone. This is thought to trigger activation of the reproductive axis by increasing the production of Kisspeptin in the arcuate nucleus (ARC) and/or by altering the expression of gonadotropin inhibiting hormone (GnIH; not shown); Kisspeptin is not present in birds and puberty onset may be primarily due to GnIH action. Photoperiodic changes also trigger anterograde action (purple dashed oval), in which seasonal prolactin (PRL) is secreted from lactotrophs in the pars distalis, driving the pelage/moult cycle. Tachykinins (TAC1) and endocannabinoids (2-AG) have been proposed to stimulate PRL secretion. Although fish do not possess an anatomically distinct pars tuberalis, the saccus vasculosus acts as seasonal sensor and signaling pathways appear largely conserved across vertebrates.

short-day photoperiod, but pelage moult to a winter coat is unaffected (Barrett et al. 2007). However, the shortening melatonin signal on the PT also appears to affect seasonality via an anterograde pathway that affects prolactin release from the pars distalis (PD) (Dardente et al. 2019). Specifically, melatonin acting on its receptors in the PT alters splicing of vascular endothelial growth factor (VEGF), which stimulates vessel growth in the infundibulum during the non-breeding season, aiding vascular communication among the PT, pars distalis (PD), and brain (Castle-Miller et al. 2017). Further, VEGF acts on VEGF receptors on lactotrophs in the PD, allowing for seasonal control of lactotroph function, altering the secretion of prolactin (Castle-Miller et al. 2017). Prolactin, in turn, controls the timing of hair and feather moult, as well as horn/antler growth (Lincoln 1990; Dawson 2006).

Photorefractoriness and circannual clocks

Although direct responses to photoperiod are critical to seasonal timing, many animals eventually fail to be stimulated by a particular photoperiod and they become photorefractory, reverting to their unstimulated physiological state (Nicholls et al. 1988). For example, while long days trigger gonadal growth and reproduction in birds that initiate reproduction in spring, their breeding seasons are often short, with gonadal regression occurring spontaneously weeks later while the days are still long. Similarly, many mammals will become refractory to the inhibitory effects of short days and spontaneously undergo gonadal growth and maturation in preparation for the breeding season. At the more extreme end of the spectrum, some vertebrates exhibit circannual rhythms in which they periodically cycle between seasonal physiological states without exposure to changing photoperiods (Pengelley and Fisher 1957; Gwinner 2012). This physiological trait is likely particularly important for species that periodically sequester themselves in hibernacula, such that they are not always exposed to photoperiodic cues. However, even species that exhibit robust circannual rhythmicity require exposure to a changing photoperiod at certain stages of the annual cycle to maintain synchrony with the natural environment—circannual rhythms under constant conditions are typically much less than 365 days, indicating the circannual clock must be entrained by photoperiodic cues (Pengelley and Fisher 1963; Gwinner 2012).

Although the existence of circannual clocks has been known for >60 years, the molecular underpinnings of the circannual mechanism remain unknown. However, in recent years it has been proposed that the PT of the pituitary may be the site of such a clock, driving seasonal endocrine circuitry in the hypothalamus and pituitary (Wood and Loudon 2018). This is supported by evidence that the retrograde T3 signaling pathway becomes spontaneously activated without exposure to a changing photoperiodic cue in photorefractory mammals (De Miera et al. 2014; Wood et al. 2015).

Perception and transduction of non-photic cues

Although evidence for the role of photoperiodic mechanisms (and photorefractoriness) in driving seasonal cycles is overwhelming across vertebrates, it is also clear that most vertebrates utilize supplementary cues to fine-tune their seasonal timing (Shutt et al. 2019; McLean and Guralnick 2021). This sensitivity to non-photic cues allows for interannual plasticity, which is likely critical to adjusting timing in response to variability in climatic conditions. Further, some animals disperse large distances from natal areas during their lifetime (or across only a few generations) and thus must be capable of correctly adjusting seasonal timing of life-history events to local conditions. Responses to non-photic cues requires sensory systems to detect and transduce cues into neural and endocrine signals that are used to adjust seasonal timing. Temperature, for example, is known to alter endogenous and photoperiod-regulated neuroendocrine mechanisms driving seasonality in vertebrates (Caro et al. 2013; Chmura and Williams 2022). Temperature perception occurs through cutaneous transient receptor potential (TRP) neurons and cold-sensing glutamate receptors (GluK2) that transmit signals to the hypothalamus, although the occurrence, sensitivity, and function of these receptors varies widely across taxa (Gracheva and Bagriantsev 2015; Gong et al. 2019). Effects of temperature appear to manifest via alterations in the same retrograde T3 signaling pathway that is activated/inactivated via photostimulation and refractory processes; TSHß, DIO2, and DIO3 have all been shown to be affected by temperature treatments, for example, though effects vary substantially across taxa (Ikegami et al. 2015; Trivedi et al. 2019; Renthlei et al. 2021; van Rosmalen et al. 2021). To date, however, there are insufficient data to predict how individuals, populations, or species will respond to climate-driven changes in ambient temperature under free-living conditions. One major issue is that studies differ substantially in the amplitude and duration of temperature manipulations applied, such that it is unclear whether differences across studies reflect taxonomy or experimental conditions (reviewed in Chmura and Williams 2022). Further, most studies in endotherms use only two temperature treatments and we caution against prediction based on two endpoints, as effects of temperature may be nonlinear.

In addition to temperature, seasonal timing can be sensitive to the availability of conspecifics, food, water, and other resources. Vertebrates often align their timing with conspecifics and the social cues have been shown to alter the timing of reproductive development through the regulation of reciprocal switching of hypothalamic Dio2/Dio3 (Perfito et al. 2015). Increased food availability often results in more rapid gonadal development and earlier breeding, although many of these effects likely occur through changes to energy balance and energy/nutrient stores (Williams et al. 2017). Hormones associated with signaling metabolic state, such as leptin and ghrelin, have known central effects on the reproductive axis (Tena-Sempere 2013). Further, low and/or variable food availability can alter circulating levels of glucocorticoids, which, in turn, may alter timing through effects on hypothalamic rf-amides, inhibition or stimulation of gonadotropin release from the pituitary, or direct effects on the gonads (Lattin et al. 2016; Chmura et al. 2020). Finally, the timing of seasonal reproduction is not solely dependent on when animals undergo seasonal puberty and mate. For example, adjusting the length of gestation is an important mechanism for altering the timing of birth in large mammals (Berger 1992). Although the mechanisms that underlie this plasticity are not well understood, direct effects of metabolic rate appear to play a role in at least some cases (Williams et al. 2017).

Over the last 10–20 years, significant progress has been made in understanding the mechanistic basis of seasonal timing, particularly with respect to reproductive timing. However, these same studies reveal diversity in taxonomic responses due to variability in cue sensitivity, as well as differences in how environmental information is integrated by internal signaling pathways. This diversity in molecular machinery likely explains the difficulty in predicting organismal responses, which has substantial implications for population, species, and community-level consequences of climate change.

Ecological implications of phenological shifts

We are gathering considerable evidence that climate change negatively impacts biodiversity (Parmesan and Yohe 2003; Chen et al. 2011; Lenoir and Svenning 2015), drives population declines (Both et al. 2010; Spooner et al. 2018; Halsch et al. 2021), and increases susceptibility to local extinction (Román-Palacios and Wiens 2020). Typically, effects of climate change on individual species are projected using species distribution models, which incorporate climatic variables and species presence/absence data (Porfirio et al. 2014). However, these models rarely consider variability in life history traits, which is key to individual success and population-level resilience (Urban 2015). Fortunately, long-term studies that examine the mechanisms that govern wildlife responses to climate change have been on the rise (e.g., Boutin and Lane 2014). These studies reveal how animals respond to a changing climate, via shifts in behavioral traits (Bastille-Rousseau et al. 2018), physiological states (Naya et al. 2017), and vital rates (Cordes et al. 2020). Phenological shifts, in particular, constitute one of the most obvious consequences of climate change, yet, the timing of life history events (e.g., timing of migration, reproduction, hibernation, or diapause patterns) remains poorly understood *in natura*, and ecologists have been challenged in their ability to explain current phenological patterns, as well as predict how such patterns may change as our climate continues to warm (Chmura et al. 2019). Some of these recent advances in our ability to Measure, Understand, and Predict phenological shifts in light of climate change (i.e., the "MUP" approach, Jenouvrier 2013) have been made possible by the cumulation of long-term, individual-based data collected over multiple decades that we have only recently began to exploit (Clutton-Brock and Sheldon 2010).

Timing of life-history events—phenological (mis)match

Phenological responses and their fitness consequences are often due to biotic interactions within and across trophic levels (Torre Cerro and Holloway 2021), rather than being simple outcomes of responses to changes in the abiotic environment. When considering the timing of phenological life history events such as reproduction, hibernation, and migration timing, synchronizing these events with the needed resources set by a seasonal environment is often referred to as a phenological match (Visser and Both 2005; Visser 2008).

The original match–mismatch hypothesis dates back to Cushing's work in fisheries as a way to explain variability in fish stock population recruitment rates (Cushing 1969). This hypothesis postulates that the consumer should temporally "match" peak energetic demands to the peak in resource availability, with any change to the relative timing of the interaction resulting in a "mismatch." It has been recently argued that "much of the difficulty in predicting the consequences of climate change-driven shifts in synchrony is due to a disconnect between ecological theory and current empirical approaches" (Kharouba and Wolkovich 2020). Yet, the authors proceed to list more than 40 studies that have done just that under the very specific criteria imposed by their review (table 1 in Kharouba and Wolkovich 2020).

Fitness consequences of a mismatch

Amongst the numerous examples of phenological mismatch that have been studied in light of climate change, one notes that the fitness consequences of shifts in phenology are not restricted to a trophic mismatch, and a number of studies have solely focused on the functional relationship that exists between phenology and demography (Post et al. 2008; Plard et al. 2014; Doiron et al. 2015).

Studies focused on mammalian hibernators, for instance, have shown significant shifts in life history traits (e.g., phenology of hibernation) and vital rates (e.g., over-winter survival rates) in response to climate change (Lane et al. 2012; Rézouki et al. 2016; Cordes et al. 2020). These life history and demographic responses may occur for a number of reasons specific to mammalian hibernators, including limited dispersal ability (Schloss et al. 2012); reduced metabolic ability to hibernate with warming-induced changes to dietary plant fatty-acids (Frank 2011); diminished metabolic savings with higher ambient temperatures (Frank 2011); and decreased reproductive allocation from depleted over-winter energy stores (Williams et al. 2015). Warming trends appeared to yield consistently positive effects on hibernator reproduction, increasing both fertility (Fietz et al. 2004; Paniw et al. 2020) and reproductive output (Schwanz 2006; Fietz et al. 2020). However, drying trends that reduce winter snowpack may erode female body condition and subsequent reproductive success (Tafani et al. 2013). Consistent with other reviews (Boutin and Lane 2014), Wells et al. (2022)found that warmer temperatures are reliably advancing hibernator phenology, and generally increasing reproductive success with longer growing seasons. By contrast, warming and drying trends are having uncertain effects on body condition, and complex effects on survival—depending on the life history, season, age class, latitude, and elevation considered.

A number of ecological and demographic studies have also focused on the impacts of climate change on nesting phenology of herbivores as it relates to plant availability and composition (Aubry et al. 2013; Doiron et al. 2015). In the Hudson Bay Lowlands, an overabundant breeding population of lesser snow geese, *Chen caerulescens caerulescens*, has dramatically damaged the ecosystem, with cascading effects at multiple trophic levels. In addition, warming of this region has widened the gap between goose migration timing and plant green-up. Warmer than average winters and summers result in lower gosling body condition and first-year survival. Too few plant "growing days" in the spring relative to hatch led to similar results, indicating that warming has widened the gap between goose migration timing and plant green-up, and this "mismatch" between goose and plant phenologies in turn affects gosling development and survival to adulthood (Aubry et al. 2013).

One cannot discuss phenological mismatch without highlighting the now-classic work that has been done across Europe on great tits (*Parus major*). In these parts, populations of great tits have exhibited a range of phenological responses to changes in spring climatic conditions (Visser et al. 2006). Because great tits rely heavily on caterpillars during the breeding season to feed their chicks, and because caterpillar biomass typically shows a narrow seasonal peak within most of Europe's oak forests (Visser et al. 2006), great tits use early spring temperatures as cues to adjust their egg-laying dates to match the seasonal peak in caterpillar biomass (Schaper et al. 2012). But in the Netherlands, for example, advancements in laying dates in response to warmer springs have been insufficient to keep pace with stronger advancements in caterpillar phenology, and the population now breeds much later relative to the seasonal caterpillar peak (Visser 2008). In years of mismatch, the probability of double-brooding, fledgling success, offspring recruitment probability, and the number of recruits were all negatively impacted. Despite strong effects on multiple reproductive components of fitness, the mismatch had no effect on adult survival, and weak effects on mean demographic rates across years. Compiling such effects on population dynamics will be essential in predicting population resilience or collapse in light of continuing warming trends brought about by climate change (Reed et al. 2012).

Trophic and food-web mismatch

Through interspecific relationships, phenology is linked to nearly all levels of biological organization, from individuals to ecosystems (Forrest and Miller-Rushing 2010). But the nature of these trophic interactions can help predict whether a mismatch could benefit one species at the detriment of the other, as opposed to systematically harming all species involved in the interaction. For instance, in antagonistic trophic interactions, mismatch will have positive fitness consequences for one of the species and negative impacts for the other (Renner and Zohner 2018). Trophic mismatch among herbivores and their food plants or among predators and prey is therefore expected to be beneficial to the prey and detrimental to the consumer (Renner and Zohner 2018). In mutualistic interactions, mismatch will have negative consequences for both species involved and should therefore be selected against. Within more complex networks, mismatched interactions may benefit or harm other mutualists or antagonists, depending on the degree of interdependence among species (Benadi et al. 2014).

Revisiting the example of lesser snow geese breeding in the Arctic Hudson Bay lowlands, Rockwell et al. (2011) examined the potential impact of changes in the extent and pattern of polar bear egg predation on lesser snow goose abundance. They used projection models that account for the increased phenological overlap of the two species but also for autocorrelation and stochasticity in the processes underlying polar bear onshore arrival and snow goose incubation phenologies. Egg predation by polar bears is predicted to reduce reproductive output of nesting lesser snow geese and lead to a reduction in the size of their nesting population on the Cape Churchill Peninsula. Stochasticity associated with these coupled phenologies will lead to periodic mismatches, allowing snow goose abundance to increase periodically (Rockwell et al. 2011). In this example, the antagonistic relationship between predator and prey is expected to benefits the predator and not entirely decimate the prey given future warming scenarios.

Plastic versus evolutionary responses

Studies focused on phenological plasticity typically document how species have responded to climate change, then use this information to make predictions about how they will continue to respond in the near future. There are four main mechanisms by which animal populations have generally responded to rapidly changing environments: (i) individuals and populations may stay put and persist locally because key phenotypes are plastic enough to withstand local changes in their environment, within physiological limits (i.e., phenotypic plasticity); (ii) populations may adapt to new conditions (i.e., niche evolution); (iii) individuals may disperse and collectively shift the population's range distribution (i.e., niche tracking); or (iv) populations may persist locally but fade to low numbers and risk demographic stochasticity, and ultimately, local extinction (Waldvogel et al. 2020). Phenological shifts are amongst the most obvious responses of animal populations to climate change (Parmesan and Yohe 2003), and while some populations may fail to respond, others may respond in ways that are either maladaptive or adaptive. Two processes can be invoked when noticing the latter: phenological

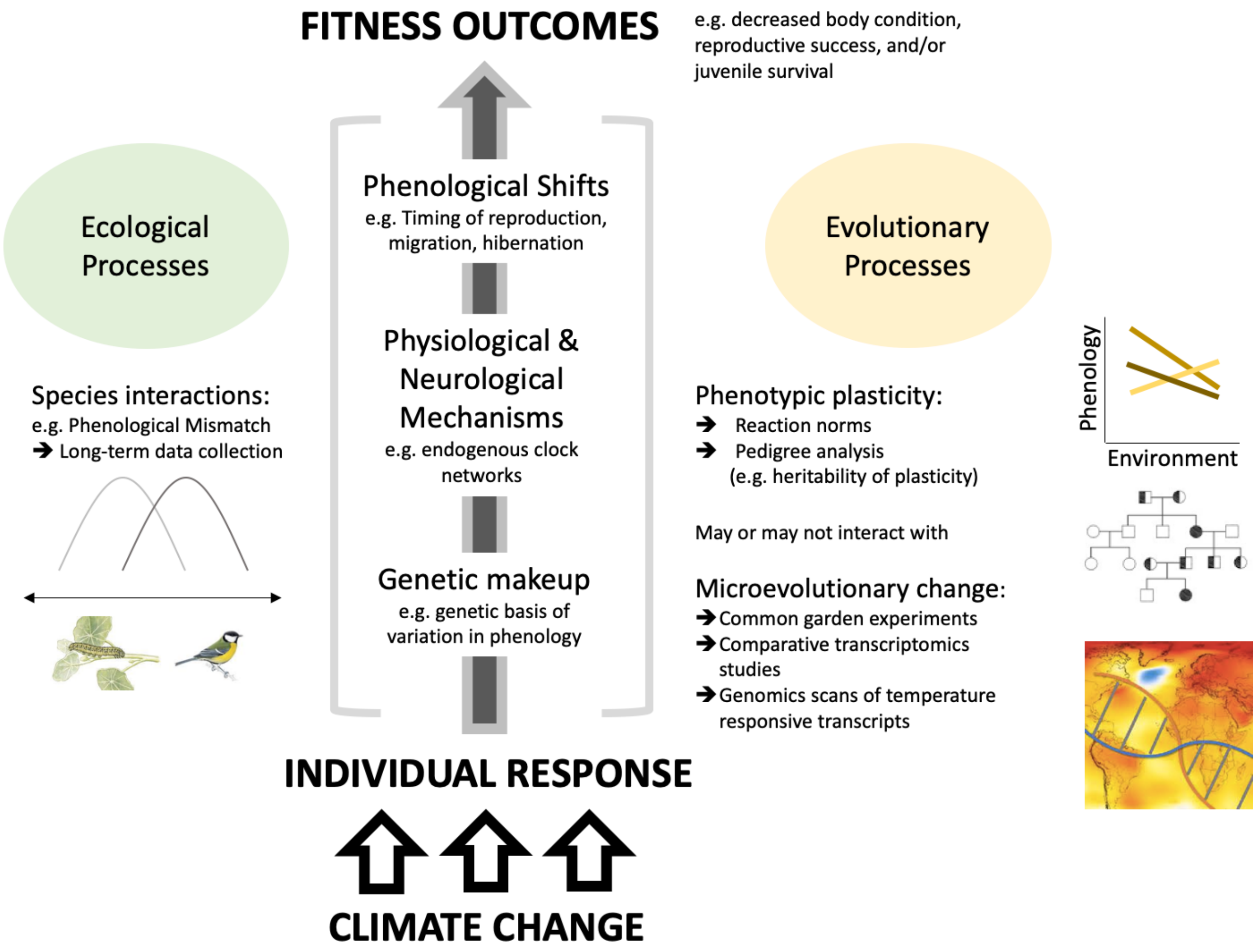

Fig. 3 Observed effect of climate change on individual phenological responses driven by genetic, neurological, and physiological mechanisms that collectively, or in isolation, can influence fitness outcomes. These mechanisms can be mediated by both ecological (e.g., phenological mismatch) and evolutionary processes (phenological plasticity, microevolution change, and their interaction) as described herein. Field, Lab, and computational approaches used to study these mechanisms are highlighted following the bold arrows.

plasticity (i) can help organisms cope with ever-changing environmental conditions at any point in time, while evolutionary change (ii) can sometimes take place when natural populations have the opportunity to at least partly adapt to a new local and selective environment (Endler 1986). This can happen on timescales as short as a few generations, then referred to as microevolution (Reznick and Ghalambor 2001). (i) and (ii) are also connected through complex eco-evolutionary dynamics and feedbacks that are extremely difficult to track in wild populations (Lane et al. 2018).

Phenological plasticity, or the ability of an organism to alter phenological traits to meet new environmental conditions (Pigliucci 2001), is a widespread phenomenon in nature (Scheiner et al. 2004) that is not always adaptive but can provide immediate fitness benefits to a rapidly changing environment (Fig. 3). Within the context of climate change, phenological traits have been shown to represent a major phenotypic response to rapidly warming and drying conditions (Walther et al. 2002; Visser and Both 2005; Radchuk et al. 2019), and a number of studies have observed that plasticity in phenological traits allows for rapid responses to climate change in the wild (e.g., Hughes 2000; Walther et al. 2002; Parmesan and Yohe 2003; Root et al. 2003; Dunn 2004; Nussey et al. 2005; Vedder et al. 2013; Charmantier and Gienapp 2014).

Traditionally, the study of phenotypic plasticity—a plastic reprogramming of unchanged genomic basis that allows individuals to respond to environmental change (Aubin-Horth and Renn 2009)—is achieved through the study of reaction norms. Reaction norms depict the range of phenotypes a single genotype can produce in response to changing environmental conditions within phylogenetic constraints. They can differ for different individuals within a population, and while some traits differ very little based on the environment, others do not differ at all (Stearns 1992). Reaction norms give us information on the degree of phenotypic plasticity (e.g., phenological plasticity) an organism can display and can help make predictions on the climate niche breadth of individual species as well as vulnerability to global climate change (Calosi et al. 2008).

Microevolutionary responses

Phenotypic plasticity allows organisms to maximize fitness as they track the predictable cycles of contrasting ecological conditions (Piersma and Van Gils 2011). But what happens when these cycles become unpredictable and place divergent selective pressures on an organism's phenological traits, such as the timing of breeding in birds, the timing of migration, or hibernation phenology? Although phenological plasticity can be heritable and may be a mechanism by which organisms can buffer themselves against the negative impacts of climate change, evolutionary processes may still provide the best protection against these negative impacts when environmental change exceeds plasticity in phenotypic traits (Gilg et al. 2012), including phenological traits. As the environmental context changes, the selective forces that define this "evolving" context—no pun intended—can shape individual fitness, vital rates (e.g., age-specific reproductive success, annual survival) and eventually drive adaptation (Fig. 3). Climate-driven genetic change in phenological traits has been documented in a number of species and phenological traits (e.g., the timing of reproduction [Bradshaw and Holzapfel 2001; Réale et al. 2003], the timing of migration [Pulido and Berthold 2010], and diapause patterns in mosquitoes [Bradshaw and Holzapfel 2008]). Yet, the lack of empirical genetic data on such traits impairs our ability to build predictive models of resilience to climate change (Urban 2015).

Microevolutionary change in phenological traits may help attain long-term viability of populations, beyond temporary fitness gains often granted by plasticity (Visser 2008). But Lane et al. (2018) warn us of how exceptionally difficult it is to distinguish between phenotypic plasticity and microevolutionary change in phenological traits. Yet, models that do not account for micro-evolution or plastic responses tend to predict a severe decline in population numbers, when adapting or plastic populations may be more buffered against such changes (e.g., Berteaux et al. 2004; Charmantier et al. 2008; Reed et al. 2010), hence the importance of quantifying both phenomena and their respective roles in helping wild animal populations track climate change via plastic and genetic shifts in phenology. Further, phenological plasticity itself may be under selection—adaptation to climate gradients over space involve divergence in plasticity indicating that adaptive responses to climate change will also likely involve the evolution of plasticity (Kelly 2019).

Revisiting our classic study of great tits in the Netherlands and United Kingdom, we know caterpillars are great tits' primary food, essential for both breeding adults and nestlings. Caterpillar phenology has been advancing at a greater rate than the reproductive phenology of great tits (e.g., hatching dates and timing of nestling food provisioning are not catching up), leading to great tit fitness declines (Visser 2008). A phenological response would be adaptive if fitness in the population was maintained following climate change. Such an adaptive response can occur if each individual responds in a way that maintains their fitness (i.e., adaptation through phenotypic plasticity) or if individuals with certain genotypes (e.g., earlier breeders) experience higher fitness and thus contribute a greater proportion of surviving young (i.e., adaptation through microevolution). In the former, selection on the trait would remain unchanged if all individuals respond appropriately and to the same degree, whereas in the latter, selection would increase (Boutin and Lane 2014). In this example, great tit populations are advancing their phenology, but to an insufficient degree so as to keep pace with their primary food source, therefore, although the direction of great tit phenological response may be adaptive, the pace is not. "A fully adaptive response would have both a sufficient direction and pace" (Boutin and Lane 2014).

Conclusions and future directions

In many species, the timing of annually recurring life-cycle events is being affected by climate change, and this has been linked to ecological mismatches and population declines. However, understanding the consequences of phenological shifts requires combining mechanistic, ecological, and evolutionary approaches at a variety of scales, from individuals to ecosystems (Visser et al. 2010), see Fig. 3. From a mechanistic standpoint, studies of free-living animals are needed to determine the predictability of phenological shifts in response to changes in the abiotic and biotic environment (McLean and Guralnick 2021), whereas controlled experiments are needed to better understand how non-photic cues are used to adjust timing (Tena-Sempere 2013; van Rosmalen et al. 2021).

Combining experimental approaches with cutting edge molecular techniques, such as single-cell RNA sequencing, will help in delineating the neurobiological mechanisms that underlie intra- and inter-specific variation in phenological responses. In addition, reductions in sequencing costs now allow for the use of genome-wide association scans (GWAS) to identify the genetic basis of variation in timing in both free-living and captive populations (Grabek et al. 2019). Using these approaches across altitudinal and latitudinal clines will likely provide insight into the genetic basis of adaptations in timing systems. Combining experimental manipulations with GWAS may prove useful in identifying the genes that underlie phenological plasticity. In addition, genome-wide approaches focused on artificial selection lines for phenological traits can provide insight into the genetic underpinnings of microevolutionary changes in seasonal timing (Mäkinen et al. 2019; Viitaniemi et al. 2019).

It is not surprising that one of the few wild vertebrate examples we could find where researchers have attempted to identify the genomic basis of seasonal timing involves the great tit—caterpillar—oak tree study system in the Netherlands and the United Kingdom. Gienapp et al. (2017) genotyped 2045 great tit females for 384,081 single nucleotide polymorphisms (SNPs) and tested for associations between SNPs and egg-laying dates. Further, da Silva (2020) subsequently tested for genome-wide associations of copy number variation (CNV) with egg-laying date in the great-tit dataset. In both studies, they failed to find any SNP or CNV that reached genome-wide significance, illustrating the challenges of identifying the genomic basis of such a highly plastic and polygenic trait. However, models that included interactions between SNP and ambient temperature consistently outperformed models without interactions, suggesting the genes responsible for within-population variation in the timing of egg-laying are dependent upon spring temperatures (Gienapp et al. 2017). The great tit—caterpillar—oak tree system illustrates the importance of long-term data collection efforts and collaboration between ecologists, evolutionary biologists, and bioinformaticians, to connect proximate (e.g., genetic basis for variation in phenological traits; endogenous clock networks), to ultimate mechanisms (e.g., fitness consequences, species interactions) in the study of phenological plasticity (Fig. 3). These efforts will most certainly benefit from increasingly affordable sequencing costs, along with the continued development of bioinformatics tools, and we encourage field biologists to collect and archive tissue samples in long-term monitoring studies. Understanding variation in phenological responses is an important theoretical and applied challenge because phenological changes can lead to declines in individual fitness (e.g., growth, reproductive success, survival) and ultimately drive local declines in population abundance that may have community—via species interactions—and ecosystem consequences resulting from trophic cascades. Although phenological plasticity is commonly evoked as a mechanism by which individuals can buffer themselves against the negative impacts of climate change, such plasticity can be maladaptive, or quickly reach the limits of possible organismal responses to climate change. It's been argued that plasticity alone will not be enough to keep up with warming conditions and adaptation via genetic change needs to take place to give vulnerable species a chance to withstand climate change in the near future (Visser 2008). A couple of approaches have been effective in measuring genetic change in response to climate change. When experiments are not feasible, as is often the case when studying species in the wild, the analysis of long-term pedigree data using quantitative genetics can help estimate the breeding value of a given trait for each individual in the studied population. By quantify trends in the "estimated genetic merit of individuals as ascertained from the phenotypes of their relatives," one can then confirm genetic change in phenological traits in response to warming conditions (e.g., Bonnet et al. 2019). But such data is hard to come by and difficult to collect. Genomic breeding values estimated from selective sweeps in the genome provide a "snapshot" alternative to long-term data collection where phenotypes are associated with genes near the genomic locations of these sweeps (Bosse et al. 2017). However, knowledge of the genes involved in shaping phenological responses is necessary for this approach to deliver.

The accumulation of long-term, individual based data; the use of natural experiments along elevation gradients that capture a breadth of climatic niches; and an improved understanding of the demographic, ecological, and evolutionary mechanisms by which interactive species respond to warming and drying trends *in natura* will collective help predict how species may respond to a warming climate via shifts in phenology.

Acknowledgments

We are grateful to all of the symposium participants, including invited speakers, complimentary session speakers, and audience members for productive discussions before, during, and after the symposium. We also thank the SICB 2022 organizers and the Divisional officers for providing support. Suzanne Miller was a joy to work with and we thank her for helping organize symposium manuscript contributions to ICB.

Funding

This work "Phenological Plasticity: From Molecular Mechanisms to Ecological and Evolutionary Implications" was supported by the National Science Foundation [grant number IOS-2137415] and the Company of Biologists. Additional support was provided by the Division of Neurobiology, Neuroethology, and Sensory Biology, the Division of Animal Behavior, the Division of Comparative Physiology and Biochemistry, the

Division of Evolutionary Developmental Biology, and the Division of Ecology and Evolution of the Society of Integrative and Comparative Biology.

Conflict of interest

The authors have no conflict of interest to report.

Data availability statement

This review paper did not utilize any data.

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