Liddle, T. A., Stevenson, T. J. and Majumdar, G. (2022) Photoperiodic regulation of avian physiology: from external coincidence to seasonal reproduction. *Journal of Experimental Zoology Part A: Ecological and Integrative Physiology*, 337(9-10), pp. 890-901.

Liddle, T. A., Stevenson, T. J. and Majumdar, G. (2022) Photoperiodic regulation of avian physiology: from external coincidence to seasonal reproduction. *Journal of Experimental Zoology Part A: Ecological and Integrative Physiology*, 337(9-10), pp. 890-901, which has been published in final form at: 10.1002/jez.2604

Title: Photoperiodic regulation of avian physiology: from external coincidence to seasonal reproduction.

Authors: Timothy Adam Liddle[1]*, Tyler John Stevenson[1], Gaurav Majumdar[1]

[1]Laboratory of Seasonal Biology, Institute of Biodiversity, Animal Health and Comparative Medicine, University of Glasgow, Glasgow UK

Correspondence: 2298191L@student.gla.ac.uk

Running Title: Photoperiodic regulation of avian seasonality

Disclosure statement: The authors have nothing to disclose

Data availability statement: The data that support the findings of this study are available from the corresponding authors upon reasonable request

Conflict of interest statement: The authors confirm that they have no conflicts of interest

Research highlights:

- Two pathways are involved in the external coincidence of avian photoperiodism, a light-detection and an interval timer pathway.
- D- and E-Box binding motifs in *EYA3* suggest and connection between the circadian clock and initial photoinduction.

ABSTRACT

Seasonal cycles of environmental cues generate variation in the timing of life history transition events across taxa. It is through the entrainment of internal, endogenous rhythms of organisms to these external, exogenous rhythms in environment, such as cycling temperature and daylight, by which organisms can regulate and time life history transitions. Here, we review the current understanding of how photoperiod both stimulates and terminates seasonal reproduction in birds. The review describes the role of external coincidence timing, the process by which photoperiod is proposed to stimulate reproductive development. Then, the molecular basis of light detection and the photoperiodic regulation of neuroendocrine timing of seasonal reproduction in birds is presented. Current data indicates that vertebrate ancient opsin is the predominant photoreceptor for light detection by the hypothalamus, compared to neuropsin and rhodopsin. The review then connects light detection to well characterized hypothalamic and pituitary gland molecules involved in the photoperiodic regulation of reproduction. In birds, Gonadotropin-releasing hormone synthesis and release is controlled by photoperiodic cues via thyrotropin-stimulating hormone-β (TSHβ) independent and dependent pathways, respectively. The review then highlights the role of D-box and E-box binding motifs in the promoter regions of photoperiodic genes, in particular Eyes-absent 3, as the key link between circadian clock function and photoperiodic time measurement. Based on the available evidence, the review proposes that at least two molecular programs form the basis for external coincidence timing in birds: photoperiodic responsiveness by TSHβ pathways and endogenous internal timing by gonadotropin synthesis.

Keywords: Birds, photoperiod, opsins, coincidence, GnRH

Introduction:

Annual seasonal changes encompass a wealth of environmental cues which may contribute to timing seasonal physiology and include ambient temperature, nutritional availability, and the changing length of daylight (Nichelmann et al 1999, Helm and Gwinner 1999, Helm and Gwinner 2005, Flinks et al 2008, Helm et al 2009). This is especially true for migrating birds in which the timing of life history transitions is dependent on the monitoring and response to changing environmental conditions over time (Gwinner and Dittami 1990, Raess and Gwinner 2005, Helm 2009). The annual change in daylength is the predominant predictive cue that birds used to time seasonal rhythms (Dawson et al., 2001; Tolla & Stevenson, 2020). Of all the avian models currently in use for the study of photoperiod and reproductive development, few are more studied than Japanese quail (*Coturnix japonica*) and migratory buntings (Huss et al 2008, Kumar et al 2021). Japanese quail show incredibly robust changes in reproductive physiology and in their neuroendocrine response to increased photoperiod (Stevenson et al 2022). Buntings show similar photoperiod response dynamics, especially within their reproductive phenotypes. Unlike Japanese quail, the effects of photoperiod on migratory behaviour have been documented in buntings (Tewary and Kumar 1982a, Kumar and Tewary 1983, Kumar et al 2002, Rani et al 2005, Majumdar et al 2014, Singh et al 2020). This review will primarily use literature derived from quail and bunting species to describe the mechanistic basis of photoperiodic time measurement through coincidence timing and seasonal reproduction.

Seasonal rhythmicity in physiology can also occur in the absence of proximate photoperiodic and supplementary environmental cues. Birds possess an internal seasonal clock, referred to as a circannual clock, that generates a nearly annual rhythm (Gwinner 1977, Berthold 1984). Endogenous circannual clocks in birds maintain their rhythmicity under constant environmental conditions (Gwinner 2003). Both the initial activation and synchronisation/entrainment of these circannual rhythms are dependent on aspects of the environment, and most notably the experienced photoperiod. Hence, the timings of avian life history events (migration, reproductive investment etc.) are synchronised by seasonal photoperiodic changes (Follett 2015). Gwinner and colleagues experimentally demonstrated the significance of photoperiod on the timing of migration in white-crowned and golden-crowned sparrows (Gwinner et al 1971). Upon the reduction of photoreception by application of a black hood or injection of black ink under the skin of the head, birds showed lower levels of migratory restlessness (*zugunruhe*) than control groups. Similar work by Donald Farner further highlights the entrainment of avian rhythms in neuroendocrinology and reproductive physiology (Farner and Wingfield 1980, Hiatt et al 1987) in white-crowned sparrows and other migratory passerines.

Internal timekeeping mechanisms are key for the successful timing of seasonal life history transition events, but also for the monitoring and regulation of several biological processes. These internal clocks may be based upon cycles of hormone secretion but may also be dependent on the control of regulatory calendar clock gene expression (Lincoln et al 2003). The circadian clock is often used to explain how daily changes in light duration are integrated at a cellular level (Green and Besharse 1996, Millar 2004, Goto 2013). Thus, the interplay between circadian clocks and seasonal interval timers entrained by photoperiod is of particular interest, given the ability of circadian clock genes to code light information (e.g., duration) and induce physiological responses. The circadian clock is therefore a critical component for timing the photoperiodic control of seasonal reproduction. This review will first cover endogenous circannual timing and external coincidence timing of light cues for the photoperiodic timing of seasonal reproduction in birds. Then, the review will describe the molecular steps from light detection by brain photoreceptors to the seasonal variation in the Gonadotropin-releasing hormone (GnRH) system. Lastly, we will discuss the role of circadian clock genes and distribution of genome binding motifs, D- and E-boxes, as a link between coincidence timing of light cues and circadian clock gene pathways.

Circannual oscillations and photoperiodic timing in birds

Endogenous circannual rhythms are particularly widespread among avian taxa, but are also present within mammals, plants, and even plankton (Harris 1963, Zamm et al 2016). Entrainment of these rhythms by photoperiod allows birds to respond with significant physiological change during the transitions between life history events. While the entrainment of circannual rhythms has been well documented within birds, and particularly within temperate birds, where photoperiodic variation is relatively great, this entrainment is less pronounced in other geographical areas (Gwinner 1977). Within equatorial latitudes, where temperature and photoperiod remain relatively constant, native birds and migrants to these environments are unable to rely on the variability of these factors to entrain their endogenous pacemakers. Here, avian breeders show asynchronous circannual rhythms, as opposed to rhythms which synchronise with seasonal change (Lincoln 2019). The endogenous circannual rhythms underpinning reproduction initiate at variable times throughout the year, and sometimes asynchronously with respect to conspecifics. Given the lack of environmental variation and consistently suitable conditions for breeding, tropical species such as the Sooty tern (*Onychoprion fuscatus*) display variable timing in reproductive investment (Bollen et al 2018). Therefore, such species are much more dependent on internal endogenous rhythms with annual timekeeping mechanisms and are less influenced by environmental variation (Wikelski et al 2008, Helm and Stevenson 2014). It stands to reason that these circannual endogenous rhythms provide an adaptive benefit, and may be ancestral, conserved in species which have since geographically diverged (Helm 2006). The characteristics of these circannual rhythms, and entrainment thereof by photoperiod, can be analysed experimentally.

While it is known that circannual timekeeping rhythms rely less on environmental variation, many species are known to show a synchronisation of these rhythms to environment. Helm and colleagues (2009) examined that the interplay between endogenous circannual rhythms and experienced photoperiod in European (*Saxicola rubicola*) and Siberian (*Saxicola maurus*) stonechats under both constant and changing light conditions. It was found that both variants of stonechats respond to photoperiod in accordance with what is expected based on their circannual timekeeping, and hence their expected geographical location. The predominant migratory behaviour used to assess circannual rhythmicity is the nocturnal zugunruhe or ‘restlessness’ displayed by many captive songbirds. Patterns of zugunruhe appear to align in period of activity and in direction of restlessness when compared to migratory conspecifics in the wild. Captive stonechats display variable timing of zugunruhe with a lack of periodicity, demonstrating sensitivity to entrainment by photoperiod (Helm 2006, Helm and Gwinner 2006). However, the observed patterns of zugunruhe are similar when comparing European migrants with African residents in captivity. Therefore, the differences in zugunruhe observed between these groups outside of captivity are highly dependent on the experienced photoperiod. Similarities between these endogenous free-running cycles in captivity indicate similar underlying programs. Differences between migrants and non-migrants arise during the expression of migration, rather than within endogenous cycles underpinning migration. This research suggests that rhythmic zugunruhe is ancestral, conserved within present-day non-migratory stonechats. Responses to environmental change are therefore characterised by the state of an individual's circannual timekeeping resulting from entrainment. By considering the internal state of avian circannual timekeeping mechanisms, and how these mechanisms may coincide with incident light, we can begin to understand the mechanism by which birds accurately respond to stimulatory photoperiod for seasonal adaptation.

Photoperiodic Coincidence Models:

The neural and cellular mechanisms by which vertebrates both detect and respond to a critical length of photoperiod (critical photoperiod) to induce reproductive change has historically been a topic of study. Critical photoperiod is generally defined as the 24-hour light-dark ratio at which half the population of a species switches from non-stimulatory to stimulatory physiological states (Hazlerigg and Wagner 2006). Thus, a photoperiod longer than the CD is considered a stimulatory long photoperiod by the animal. The critical photoperiod length has been reported as ~11.5 hours in Japanese quail (Simpson and Follett 1982), but the critical length of photoperiod is variable among avian taxa (Dawson 1987, Rani et al 2005) and within different environmental conditions, including latitude (Silverin et al 1992). Overall, this implies a mechanism by which animals measure photoperiod length, termed photoperiodic time measurement. Two leading models have been postulated to explain the role of photoperiodic time measurement: the internal coincidence model, and the external coincidence model. The internal coincidence model describes a theoretical system in which two or more internal timers (i.e. circadian clock genes) are entrained by photoperiod. Changing daylengths may cause these timers to coincide in such a way that initiates induction of seasonal responses. In birds, this model lacks experimental support. Whilst some parties welcome the internal coincidence model as an explanation for aspects of photoperiodic timing (Underwood et al 1997, Yadav and Chaturvedi 2014), others, like Farner and Gwinner, suggested that the model is too complex or have provided experimental evidence against internal coincidence in photosensitive birds (Farner et al 1977, Meier 1981). Instead, the external coincidence model posits that the oscillating external light stimulus entrains one or more internal timers of sensitivity to annual photoperiod, and its photoinducible phase (ϕi; Figure 1). Coincidence between the photoinducible phase and a light stimulus, are required for successful induction of reproductive development. Evidence for the external coincidence model has been demonstrated in several birds (Table 1) and other taxa (Saunders 1979, Prasad et al 1982, Simpson and Follett 1982, Tewary and Kumar 1982b, Tewary and Prasad 1983, Ravikumar and Tewary 1990). The precise nature of the molecular substrates that provide interval timing for the external coincidence are described in detail below.

Photoperiodic Regulation of Seasonal Life History Transitions in birds:

In most long day breeding birds, the annual change in day length results in three distinct life-history photoperiodic states: photosensitive, photostimulated, and photorefractory (Nicholls et al., 1983; Stevenson et al., 2012). European starlings held in short days (<11.5hrs) for longer than 2 weeks results in birds that are physiologically responsive to stimulatory long days and are referred to as photosensitive (Dawson and Goldsmith 1997; Stevenson et al., 2012). In this state birds are physiologically responsive to light stimulation during the photoinducible phase (Follett et al 1992). The importance of the specific timing of light exposure on the avian response to photoperiod has often been a point of interest for researchers. Follett and Sharp showed experimentally in 1969 that the gonadal response of Japanese quail to a stimulatory photoperiod is dependent on the state of their endogenous circadian rhythm, hence why a single pulse of light during a photoinducible phase is sufficient to initiate significant reproductive change (Follett and Sharp 1969). Follett and colleagues (1974) showed that when transferring photosensitive white-crowned sparrows from a light schedule consisting of 8 hours of light, and 16 hours of darkness, to complete darkness, 8-hour pulses of light between 2 and 100 hours after lights off were sometimes able to stimulate plasma luteinising hormone (LH) concentration, indicative of a reproductive response to photoperiod (Follett et al 1974). Further, the periods of time in which these light pulses were stimulatory occurred regularly at approximately daily intervals. Hence, Follett and colleagues provided experimental evidence to suggest that not only was an underlying endogenous circadian rhythm involved in reproductive development, but also that this rhythm could be activated through stimulation by photoperiod. Similar dynamics of an endogenous circadian element in photoperiodic stimulation of reproduction were also uncovered in the house sparrow (Farner et al 1977).

The significance of the dark period during a photoperiodic cycle was explored experimentally in other species. Jenner and Engels first verified the stimulatory nature of long photoperiod (16h) in male juncos and white-throated sparrows before placing birds on a schedule of 8.25h light followed by darkness interrupted by 1.75h light in the middle of the dark (Jenner and Engels 1952). They found that this short light pulse was sufficient to induce gonadal growth and mature sperm development in males. This evidence provided empirical support for the presence of a photoinducible phase, first coined by Bünning in 1936, in the avian photoperiodic response (Bünning 1936). Light exposure during the photoinducible phase results in reproductive development during which birds become photostimulated. In this state, birds are reproductively active and engage in high rates of nest building, copulatory behaviors and egg laying (McDonald 1976, Sharp 1993). Tewary and Tripathi (1983) identified that female migratory buntings (*Emberiza bruniceps*) have significant ovarian growth when exposed to longer day lengths consistent with those observed in summer months (Tewary and Tripathi

1983). Long days also inhibit reproduction evidenced by spontaneous regression after prolonged exposure (Bentley et al., 1998). Thus, long days have a dual role to stimulate and then inhibit reproductive physiology. Reproductive involution in response to long days is referred to as absolute photorefractoriness (MacDougall-Shackleton et al., 2009). Some birds, such as the Japanese quail, maintain reproductive function on long days and don't exhibit spontaneous regression therein (Robinson and Follett 1982). Rather, a reduced photoperiod is required to initiate a reversal of reproductive investment. Therefore, photorefractoriness here is defined as relative (MacDougall-Shackleton et al., 2009).

It is known that most bird species do not require functioning retina in order to perceive light and respond appropriately to photostimulatory photoperiods, including Japanese quail (Homma et al 1972). Blinded quail exhibit the same patterns of gonadal growth upon stimulation of a long photoperiod compared to untreated birds, suggesting that the presence of extraretinal photoreceptors ~~are~~ is responsible for light detection for the seasonal response. Similar research has been performed in house sparrows, with several papers demonstrating an unchanged photoperiodic response when comparing blinded and non-blinded birds (Menaker et al 1970, Underwood and Menaker 1970). Such research has been crucial in directing research towards the discovery of deep brain photoreceptors, now known to be widespread across avian taxa (Pérez et al., 2019). The avian photoperiodic response includes three main components, (i) hypothalamic light receptors, (ii) the reproductive hypothalamo-pituitary gonadal axis, and (iii) the circadian clock. Here, we will describe the neuroendocrine signal transduction cascade, involving photostimulation of deep brain photoreceptors (opsins) and subsequent regulation on deiodinase type 2 (*DIO2*) and type 3 (*DIO3*) expression, as a photoinducible molecular link between photostimulation and GnRH expression. In this way, we propose that two pathways are involved in the external coincidence model. There is a light detection pathway that links deep brain photoreceptors with *DIO2/3* expression in tanycytes and a second interval timer pathway that resides in the GnRH-gonadotropes system. The coincidence timing of the two pathways is responsible for triggering the avian photoperiodic response.

Opsins: molecular substrates for light detection in birds

Opsins are a family of light-sensitive, G-protein coupled receptor membrane proteins. Structurally, almost all the opsins consist of a single polypeptide chain of 340-500 amino acids forming seven alpha-helical transmembrane regions with the cytoplasmic or extracellular loops and domains connecting the transmembrane regions (Palczewski *et al*., 2000). Vitamin A chromophore is an 11-cis retinaldehyde (A1) and binds to the seven-helix bundle which, when absorbing a photon of light, converts to an all trans stage by photoisomerization. This conformational change of the chromophore interacts with transducin (G-protein), triggering the photoinduction molecular cascade and change in membrane potential (Palczewski *et al*., 2000). All the photopigments have a characteristic absorption spectrum with a specific maximal sensitivity (lambda max). Three opsin classes have received the most attention due to the anatomical localization, function, and action spectrum in avian brain and include rhodopsin, neuropsin and Vertebrate Ancient opsin. Here, we will focus on the evidence to suggest the role of each photoreceptor in the control of avian photoperiodism.

Rhodopsin

Rhodopsins are classified into Type 1 molecules found in microbes like bacteria, archaea, fungi and algae and Type 2, which are the visual pigments in vertebrates and invertebrates (Palczewski *et al*., 2000). The photoreceptors in the quail brain were found to fit to an action spectrum of rhodopsin with the maximum absorption at 492nm (Foster & Follett, 1985). Rhodopsin monoclonal antibody RET-P1 identified two cell populations of rhodopsin positive neurons: in the lateral septum (SL), in the infundibular nucleus (IN), and in median eminence (ME) in ring doves (Wada *et al*., 1998). The expression of rhodopsin mRNA has also been found to increase with increased duration of light and vary in different physiological states of migratory buntings with peak expression in the photostimulated state (Majumdar *et al*., 2015b). Along with the photoperiod-dependent expression, it has also been shown that rhodopsin expression has a circadian pattern, and light pulse in the night can elevate rhodopsin expression (Korenbrot *et al*., 1989). Thus, keeping in mind that light at the photoinducible phase, which usually falls in the early evening of many bird species, induces gonadal development, rhodopsin may be one of the brain photoreceptors implicated in light detection for neuroendocrine regulation of gonadal development.

Neuropsin (OPN5)

Bioinformatic and molecular search for new opsins resulted in the isolation of neuropsin from mice and human tissues (Tarttelin *et al*., 2003). The gene shares only 20%-30% similarity with other opsin families and so has been designated as a new family. It shows all the functionally important characteristics of other opsins but along with a lysine retinaldehyde chromophore binding site in the seventh transmembrane domain (Tarttelin *et al*., 2003). Later it was shown by analyzing purified OPN5 protein that it does not act as retinal photoisomerase but functions as a UV sensitive GPCR, which couples with Gi type G protein (Yamashita *et al*., 2010). OPN5-positive cells have been found in the chicken retina, pineal gland, and paraventricular organ (PVO; (Yamashita *et al*., 2010)). Detailed localization of OPN5 in quail brain revealed its presence in CSF contacting neurons in the PVO region and in the external zone of the ME, which connects to the pars tuberalis (PT) (Nakane *et al*., 2010). Experimentally, incident light with a lambda max of 415nm can stimulate OPN5 to induce a change in voltage in *Xenopus* oocytes. It is therefore inferred that OPN5, present in CSF-contacting neurons, acts as a light sensor and subsequently generate membrane currents in response (Nakane et al 2010). In chickens, another OPN5-like gene, OPN5L2 has been shown to be present laterally in the third ventricle colocalizing with GnRH-I cells, reinforcing its probable role as a deep brain photoreceptor (Ohuchi et al., 2012). However, a direct test for the functional significance of *OPN5* in seasonal neuroendocrine events revealed an inhibitory role of this opsin on thyrotropin-stimulating hormone-β (*TSHβ*) which has a direct role in the photoperiodic gonadal induction. Injections of OPN RNAi into the ventricular system of border canaries caused an upregulation of *TSHβ* mRNA levels.

Further, the mRNA levels of *OPN5* did not change in response to light in the photoinducible phase (Stevenson & Ball, 2012). Similar observations were made in photoperiodic red headed buntings where neuropsin levels did not vary in different lengths of photoperiod, and a significantly negative correlation was found between *TSHβ* and *OPN5* expression (Majumdar *et al*., 2015a). Thus, the anatomical localization and functional considerations suggest a role of OPN5 in the photoperiodic regulated neuroendocrine system in birds, but the course of action on the mechanism is unclear.

Vertebrate ancient opsin

Vertebrate Ancient opsin (VA opsin) was first isolated from cDNA pool of salmon eye tissue with the derived amino acid sequencing showing about 37% - 42% similarity with other opsin families (Soni & Foster, 1997). Structurally, VA opsin has many similar features as of other opsins but on the third cytoplasmic domain, four non-conserved substitutions with two amino acid deletions make it unique as a photoreceptive molecule, making it a small-sized opsin with light-dependent phosphorylation properties (Soni & Foster, 1997). In birds, VA opsin has two isoforms: 972 bp VA and 1080 bp VAL, which encodes for a 323 and 359 amino acid long protein, respectively. Both proteins have been shown to be capable of eliciting a retinal dependent light response with current productions in patch clamp recordings (Halford *et al*., 2009). VA opsin mRNA have been amplified from chicken hypothalamic cDNA and antibodies against it have shown positive signal in anterior hypothalamus adjacent to the third ventricle, supraoptic nucleus, PVN and BnSTm and ME adjacent to the PT (Halford *et al*., 2009). Both isoforms of VA opsin have an approximate lambda max of 490nm, which corresponds to the previously accepted avian photoperiodic response peak at 492 nm (Davies et al., 2012).

The precise mechanistic link between light detection by opsins in the hypothalamus and the synthesis and release of GnRH from the median eminence is not well characterized. Recent work has identified a series of molecular steps during the photoinducible phase and photostimulation that provide a framework to identify potential neural circuits.

Molecular substrates that link photodetection and seasonal reproductive physiology

Photoperiodic regulation of hypothalamic~~:~~ expression of GnRH

Gonadotropin-releasing hormone-I (GnRH-I; (King et al., 1966) and GnRH-II (Miyamoto et al., 1984)) were first isolated from domestic chicken while GnRH-III was isolated from lamprey and later found in songbirds (Bentley et al., 2004). Anatomical localization of GnRH-I includes preoptic area (POA) with the fibres extending up to ME along the third ventricle and in the lateral septal area (Millam et al., 1995; Stevenson and Ball, 2009). GnRH cells expressed in the pre-optic area (POA) of the hypothalamus forms one of the most important links between the brain and the downstream reproductive physiology in birds (Gore, 2002). The annual change in photoperiod (or simulated photoperiodic changes in laboratory) causes distinct changes in the GnRH expression in many avian species (Figure 2) (Stevenson et al., 2013). This dramatic variation in GnRH expression is believed to be very pronounced in avian species in comparison to other vertebrates (Stevenson et al., 2012). Photorefractory birds exposed to short photoperiod increase GnRH after 10 days suggesting that GnRH may be the neural substrate for gaining photosensitivity (Dawson and Goldsmith, 1997; Stevenson et al., 2012). Then, photosensitive birds exposed to long stimulatory photoperiod display a further increase in GnRH synthesis that is maintained during the breeding periods. Then prolonged exposure to long days and the onset of photorefractoriness is caused by a decline in GnRH content. Other opportunistic and flexible reproductive strategies in birds maintain relatively constant GnRH content which likely functions to provide rapid changes in reproductive physiology in response to environmental conditions for optimal for breeding (MacDougall-Shackleton et al., 2009).

GnRH release is triggered by thyrotropin-stimulating hormone driven changes in Deiodinase type-2

Increased hypothalamic triiodothyronine (T3) during the photoinducible phase and the subsequent rise in the gonadotropin, luteinizing hormone mRNA expression, suggested a causal link between thyroid hormone, photoperiod, and gonadal regulation (Yoshimura et al., 2003). In quail, it was found that the common glycogen polypeptide (CGA) mRNA, which together with TSHβ forms the functional TSH hormone. In birds, induction of *TSHβ* mRNA was subsequently shown in Border canaries (Stevenson and Ball, 2012) and migratory red headed buntings (Majumdar *et al.,* 2014). Hypothalamic thyroid hormone signalling is critical for the long-day induction of GnRH release (Figure 2) (Yoshimura *et al.,* 2003). Search for molecular components in the mediobasal hypothalamus (MBH) yielded *DIO2* and *DIO3*. *DIO2* was found to be upregulated by a long photoperiod in the MBH (Yoshimura *et al*., 2003). Further analysis found a high concentration of active 3,5,3’ -triiodothyronine (T3) and prohormone thyroxine (T4) in MBH tissue in response to long days from short days, although no change was detected in plasma concentration of these hormones (Yoshimura *et al*., 2003). A causal role for TSH was established by ICV injections of a bovine TSH, which induced expression of *DIO2* in a dose dependent manner in the ependymal layer of the third ventricle (3rdV; Nakao *et al*., 2008). *DIO3* expression decreases in response to long days, the reciprocal expression of *DIO3* occurs in the MBH, but the primary activator of increased *DIO3* transcription remains unresolved; Evidence in mammals suggests an epigenetic mechanism (Stevenson and Prendergast, 2013). Along with the thyroid hormone related changes, it has also been shown that the GnRH nerves undergo huge seasonal changes in their morphology (Yamamura et al., 2004). The GnRH nerve terminals lie in very close proximity to the basal lamina in median eminence when exposed to long photoperiod and the encasement of their terminals by glial endfeet is also reduced (Yamamura et al., 2004, Nakane and Yoshimura 2010). Later it was shown that relatively higher levels of T3 reduces the amount of glial (tanycytic) processes contacting the basal lamina and that these numbers were negatively corelated with the number of neurons contacting the basal lamina (Yamamura et al., 2006). These studies indirectly support they hypothesis that changes in thyroid action due to change in photoperiod can cause morphological and anatomical changes to brain cells along with associated molecular dynamics. Altogether, these data indicate that TSHβ activation during the photoinducible phase is the primary molecular substrate for photoperiodic regulation of the external coincidence model (Figure 2). It is likely that other molecules, such as GnRH or FSHβ contribute to the endogenous internal timing for seasonal reproduction, and that regulation of these molecules is initiated by upstream TSHβ activation. Given the importance of the circadian clock in timing these molecular changes which link photoperiod and investment into reproductive physiology, it is pertinent to consider whether the clock itself plays a role in the regulation of such molecules, outside of initial timing of stimulation.

Link between circadian clock timing and photoperiodic response

The rhythmic expression of circadian clock genes is essential for the regulation and maintenance important biological functions, including immune response, hormone synthesis and release, metabolism, and sleep-wake cycles (Ikegami et al 2019). The first instance of daylight in a 24-hour cycle synchronises the circadian clock to begin its daily rhythm (Cassone 2014). It is through this synchronisation that individuals determine the beginning of their “subjective day”. The avian circadian clock possesses both positive and negative elements, which upregulate and downregulate aspects of the circadian clock itself, respectively (Dunlap 1999). The clock genes *BMAL1* (Brain and Muscle ARNT-Like 1) and *CLOCK* (Circadian Locomotor Output Cycles Kaput) are initially transcribed and translated into BMAL1 and CLOCK protein, which heterodimerize. The BMAL1/CLOCK dimer promotes transcription of clock genes *PER2* and *3* (Period protein) and *CRY1* and *2* (Cryptochrome protein, Yoshimura et al 2000, Yasuo et al 2004). Dimerization of PERs and CRYs results in a complex which interferes with BMAL1/CLOCK dimerization, acting in a negative feedback loop to reset the circadian clock. Expression patterns of the clock genes *BMAL1*, *CLOCK*, *PER2*,*3*, *CRY1*, and *2* are known to be stable within the MBH of Japanese quail under variable light conditions (Yasuo et al 2003). This allows for consistent timekeeping in the presence of photoinducible light stimuli and maintains a regular photoinducible phase. It is known that the BMAL1/CLOCK dimer regulates transcription of *CRY* and *PER* paralogues by binding to E-box sequences (CANNTG, where N = any appropriate nucleotide) within the promoter regions of target genes (Nakao et al 2007). Similarly, binding to D-box DNA cis-elements within gene promoter regions promotes transcription. Therefore, by searching for E- and D-box promoter regions upstream of a gene's start codon, we can determine whether they are likely to be regulated by the circadian clock (Helfer et al 2006, Onoue et al 2019) (Table 2-5).

When investigating the photoperiodic response, the transcription genes involved in the neuroendocrine signal transduction cascade (following exposure to a stimulatory photoperiod) is of particular interest. It is expected that if a gene is clock-controlled, their expression pattern over a 24-hour period should mirror that of their corresponding regulatory clock gene. The indication that a gene is clock-controlled provides important insight into the function of the gene and may indicate a role in coordinating a connection between photoperiod and circadian clock. D-box and E-box positions (Table 2-3 and Table 4-5, respectively) in the promoter regions of various photoperiodic genes of interest have been provided. Each relevant avian D-box and E-box motif has been cross-checked within the promoter regions of these genes of interest, and presence highlighted. These findings represent new data, suggestive of a potential link between the circadian clock and the neuroendocrine response to photoperiod. Each highlighted gene is involved to some degree in the avian neuroendocrine response to photoperiod, whether that role be in photoreception (e.g., Eyes-absent-3 (*EYA3*)) or reproduction (e.g., GnRH). Data is provided for the best characterized bird genomes: chicken (*Gallus gallus*) and Japanese quail (*Coturnix japonica*). The presence of E-Box and D-Box in the promoter region of *EYA3* in chicken and quail indicate this genomic motif is critical for linking the circadian clock and genes implicated in the initial stages of photoinduction. These data suggest that light activation during the photoinducible phase drives circadian clock gene binding to D-Box and E-Box motifs in *EYA3* and the key photoperiodic component for the external coincidence model. Despite this suggestive evidence, at this stage a solid molecular link between the avian circadian clock and neuroendocrine response to photoperiod has not been established experimentally.

EYA3 is a member of EYA gene family first identified in *Drosophilla* as a transcription factor in eye development and have two distinct domains: C terminal domain which interacts with other proteins and a tyrosine rich N terminal domain which contributes to its transactivational activity uniquely, *EYA3* has a dual function of transcription factor and has an intrinsic phosphatase activity (Rebay *et al*., 2005). Although the role of *EYA3* has been extensively studied in tissue development, recent advances also suggest a possible link with the circadian clock in mammals (Wood et al., 2020) *EYA3* mRNA expression sites include muscles, retina, and in PT in MBH of both birds and mammals (Nakao *et al*. 2008; Dardente *et al*. 2010). Recently it was also shown that EYA3 peptide is expressed at elevated levels in long day (Majumdar *et al*., 2014). With two E-box elements in promotor (making it sensitive to CLOCK and BMAL1) and two D-box elements (which makes it sensitive to TEF1 (transcriptional elongation factor 1) /SIX (sine oculis homeobox) elements), it provides support as a photoperiodic gene for the integration of external photic cues for coincidence timing (Dardente *et al.*, 2010) (Table 2-5). In birds, melatonin does not play any role in photoperiodic control of reproduction (Juss et al., 1993), *EYA3* has been suggested to be a part of the transduction of photoperiodic information pathway rather than directly involved in induction (Majumdar *et al.*, 2014). Expression of EYA3 peptide in corresponding areas where rhodopsin is expressed in the hypothalamus (Majumdar *et al.* 2014) along with the evidence that *EYA3* mRNA expression correlates with the rhodopsin mRNA expression in response to increasing photoperiods (Majumdar *et al*., 2015b) suggests that *EYA3* is directly linked with light detection for the avian photoperiodic response.

Summary and concluding remarks

Seasonal changes in photoperiod and the daily timing of light stimulation are crucial for the control of seasonal breeding in birds. The external and internal coincidence models provide explanations for the mechanism by which birds respond to photoperiod in a stimulatory manner. Despite some debate as to the more appropriate model, experimental evidence generally favours the external coincidence model, or Bünning hypothesis, as an explanation for avian photoperiodism. Circannual endogenous rhythms show similar programming between species. Expression of such endogenous cycles are altered through entrainment by photoperiod, a reliable indicator of seasonal time. Birds show a heightened reception to stimulatory photoperiods during a photoinducible phase occurring circa 11.5 hours after dawn in Japanese quail. Coincidence of a light pulse during this photoinducible phase results in neuroendocrine and physiological changes linked to reproductive investment and is particularly apparent in Japanese quail. Where species are similar in photostimulation, differences are observed in photorefraction. Japanese quail require a period of shortened days to reset their reproductive statuses (relative photorefractoriness) whereas red-headed buntings show spontaneous regression of gonads when maintained on long days (absolute refractoriness). Deep brain photoreception is widespread across avian taxa. Rhodopsin, neuropsin, and vertebrate ancient opsin have all been implicated in the avian photoperiodic response. Although the link between light reception by these opsins and the following GnRH synthesis and release from the median eminence is not fully understood, GnRH is an essential messenger that connects the neuroendocrine changes in the brain to downstream changes in reproductive physiology. The data suggest that GnRH and/or gonadotropin synthesis may act as the endogenous interval timer that connects hypothalamic responsiveness to stimulatory photoperiodic cues driven by TSHβ signalling (Figure 1).

Acknowledgements

The work was funded by a Leverhulme Trust Research Leader award to Tyler John Stevenson. Figures were created using BioRender. We would like to thank Dr Randy Nelson (Editor-in-Chief, Journal of Experimental Zoology: Part A) and Dr Gregory Demas (Associate Editor, Indiana University) for their insight and helpful comments during the review process.

References:

Appenroth, D., Melum, V. J., West, A. C., Dardente, H., Hazlerigg, D. G., & Wagner, G. C. (2020). Photoperiodic induction without light-mediated circadian entrainment in a High Arctic resident bird. *Journal of Experimental Biology*, *223*(16), jeb220699.

Bentley, G. E., Goldsmith, A. R., Dawson, A., Briggs, C., & Pemberton, M. (1998). Decreased light intensity alters the perception of day length by male European starlings (Sturnus vulgaris). *Journal of Biological Rhythms*, *13*(2), 148-158.

Bentley, G. E., Moore, I. T., Sower, S. A., & Wingfield, J. C. (2004). Evidence for a novel gonadotropin-releasing hormone in hypothalamic and forebrain areas in songbirds. *Brain, behavior and evolution*, 63(1), 34-46.

Berthold, P. (1984). The endogenous control of bird migration: a survey of experimental evidence. *Bird Study*, 31(1), 19-27.

Bollen, A., Matilde, E., & Barros, N. (2018). An updated assessment of the seabird populations breeding at Príncipe and Tinhosas. *Ostrich*, *89*(1), 47-58.

Bünning, E. (1936). Endogenous daily rhythms as the basis of photoperiodism. *Ber Deut Bot Ges*, *54*, 590-607.

Cassone, V. M. (2014). Avian circadian organization: a chorus of clocks. *Frontiers in neuroendocrinology*, 35(1), 76-88.

Dardente, H., Wyse, C. A., Birnie, M. J., Dupré, S. M., Loudon, A. S., Lincoln, G. A., & Hazlerigg, D. G. (2010). A molecular switch for photoperiod responsiveness in mammals. *Current Biology*, 20(24), 2193-2198.

Davies, W. I., Turton, M., Peirson, S. N., Follett, B. K., Halford, S., Garcia-Fernandez, J. M., ... & Foster, R. G. (2012). Vertebrate ancient opsin photopigment spectra and the avian photoperiodic response. *Biology letters*, 8(2), 291-294.

Dawson, A. (1987). Photorefractoriness in European starlings: critical daylength is not affected by photoperiodic history. *Physiological zoology*, *60*(6), 722-729.

Dawson, A. (2001). The thyroid and photoperiodism. *Avian endocrinology*.Dawson, A. (2001). Thapliyal, jp. The thyroid and Photoperiodism. In *Avian Endocronology*, 141-151.

Dawson, A., & Goldsmith, A. R. (1997). Changes in gonadotrophin-releasing hormone (GnRH-I) in the pre-optic area and median eminence of starlings (Sturnus vulgaris) during the recovery of photosensitivity and during photostimulation. *Reproduction*, 111(1), 1-6.

Dunlap, J. C. (1999). Molecular bases for circadian clocks. *Cell*, 96(2), 271-290.

Farner, D. S., & Wingfield, J. C. (1980). Reproductive endocrinology of birds. *Annual review of physiology*, 42(1), 457-472.

Farner, D. S., Donham, R. S., Lewis, R. A., Mattocks Jr, P. W., Darden, T. R., & Smith, J. P. (1977). The circadian component in the photoperiodic mechanism of the house sparrow, Passer domesticus. *Physiological Zoology*, 50(4), 247-268.

Flinks, H., Helm, B., & Rothery, P. (2008). Plasticity of moult ad breeding schedules in migratory European Stonechats Saxicola rubicola. *Ibis*, 150(4), 687-697.

Follett, B. K. (2015). "Seasonal changes in the neuroendocrine system": some reflections. *Frontiers in neuroendocrinology*, 37, 3-12.

Follett, B. K., & Sharp, P. J. (1969). Circadian rhythmicity in photoperiodically induced gonadotrophin release and gonadal growth in the quail. *Nature*, 223(5209), 968-971.

Follett, B. K., Kumar, V., & Juss, T. S. (1992). Circadian nature of the photoperiodic clock in Japanese quail. *Journal of Comparative Physiology A*, 171(4), 533-540.

Follett, B. K., Mattocks, P. W., & Farner, D. S. (1974). Circadian function in the photoperiodic induction of gonadotropin secretion in the white-crowned sparrow, Zonotrichia leucophrys gambelii. *Proceedings of the National Academy of Sciences*, 71(5), 1666-1669.

Foster, R. G., & Follett, B. K. (1985). The involvement of a rhodopsin-like photopigment in the photoperiodic response of the Japanese quail. *Journal of comparative physiology A*, 157(4), 519-528.

Gore, A. C. (2002). *GnRH: the master molecule of reproduction*. Springer Science & Business Media.

Goto, S. G. (2013). Roles of circadian clock genes in insect photoperiodism. *Entomological Science, 16*(1), 1-16.

Green, C. B., & Besharse, J. C. (1996). Identification of a novel vertebrate circadian clock-regulated gene encoding the protein nocturnin. *Proceedings of the National Academy of Sciences, 93*(25), 14884-14888.

Gupta, N. J., Kumar, A., & Bhardwaj, S. K. (2015). Photo-gonadal response of Indian brahminy myna to resonance cycles in different seasons. *Biological Rhythm Research*, *46*(1), 33-38.

Gwinner, E. (1977). Circannual rhythms in bird migration. *Annual Review of Ecology and Systematics*, 8(1), 381-405.

Gwinner, E. (2003). Circannual rhythms in birds. *Current opinion in neurobiology*, 13(6), 770-778.

Gwinner, E., & Dittami, J. (1990). Endogenous reproductive rhythms in a tropical bird. *Science*, 249(4971), 906-908.

Gwinner, E. G., Turek, F. W., & Smith, S. D. (1971). Extraocular light perception in photoperiodic responses of the white-crowned sparrow (Zonotrichia leucophrys) and of the golden-crowned sparrow (Z. atricapilla). *Zeitschrift für vergleichende Physiologie*, *75*(3), 323-331.

Halford, S., Pires, S. S., Turton, M., Zheng, L., González-Menéndez, I., Davies, W. L., ... & Foster, R. G. (2009). VA opsin-based photoreceptors in the hypothalamus of birds. *Current Biology*, 19(16), 1396-1402.

Harris, J. E. (1963). The role of endogenous rhythms in vertical migration. *Journal of the Marine Biological Association of the United Kingdom*, 43(1), 153-166.

Harris, M. O., & Turek, F. W. (1982). Photoperiodic control of the timing of testicular regression in white-throated sparrows. *General and comparative endocrinology*, *46*(1), 124-129.

Hazlerigg, D. G., & Wagner, G. C. (2006). Seasonal photoperiodism in vertebrates: from coincidence to amplitude. *Trends in Endocrinology & Metabolism*, 17(3), 83-91.

Helfer, G., Fidler, A. E., Vallone, D., Foulkes, N. S., & Brandstaetter, R. (2006). Molecular analysis of clock gene expression in the avian brain. *Chronobiology international*, 23(1-2), 113-127.

Helm, B. (2006). Zugunruhe of migratory and non-migratory birds in a circannual context. *Journal of Avian Biology*, 37(6), 533-540.

Helm, B. (2009). Geographically distinct reproductive schedules in a changing world: costly implications in captive stonechats. *Integrative and Comparative Biology*, 49(5), 563-579.

Helm, B., & Gwinner, E. (1999). Timing of postjuvenal molt in African (Saxicola torquata axillaris) and European (Saxicola torquata rubicola) stonechats: effects of genetic and environmental factors. *The Auk*, 116(3), 589-603.

Helm, B., & Gwinner, E. (2005). Carry-over effects of day length during spring migration. *Journal of Ornithology*, 146(4), 348-354.

Helm, B., & Gwinner, E. (2006). Migratory restlessness in an equatorial nonmigratory bird. *PLoS biology*, 4(4), e110.

Helm, B., & Stevenson, T. J. (2014). Circannual rhythms: history, present challenges, future directions. In *Annual, lunar, and tidal clocks* (pp. 203-225). Springer, Tokyo.

Helm, B., Schwabl, I., & Gwinner, E. (2009). Circannual basis of geographically distinct bird schedules. *Journal of Experimental Biology*, 212(9), 1259-1269.

Hiatt, E. S., Goldsmith, A. R., & Farner, D. S. (1987). Plasma levels of prolactin and gonadotropins during the reproductive cycle of white-crowned sparrows (Zonotrichia leucophrys). *The Auk*, 104(2), 208-217.

Homma, K., Wilson, W. O., & Siopes, T. D. (1972). Eyes have a role in photoperiodic control of sexual activity of Coturnix. *Science*, *178*(4059), 421-423.

Huss, D., Poynter, G., & Lansford, R. (2008). Japanese quail (Coturnix japonica) as a laboratory animal model. *Lab animal*, 37(11), 513-519.

Ikegami, K., Refetoff, S., Van Cauter, E., & Yoshimura, T. (2019). Interconnection between circadian clocks and thyroid function. *Nature Reviews Endocrinology*, *15*(10), 590-600.

Jenner, C. E., & Engels, W. L. (1952). The significance of the dark period in the photoperiodic response of male juncos and white-throated sparrows. *The Biological Bulletin*, *103*(3), 345-355.

Juss, T.S., Meddle, S.L, Servant, R.S., & King, V.M. (1993). Melatonin and Photoperiodic Time Measurement in Japanese Quail (Coturnix Japonica).” *Proceedings: Biological Sciences* 254(1339): 21–28.

King, J. R., Follett, B. K., Farner, D. S., & Morton, M. L. (1966). Annual gonadal cycles and pituitary gonadotropins in Zonotrichia leucophrys gambelii. *The Condor*, 68(5), 476-487.

Korenbrot, J. I., & Fernald, R. D. (1989). Circadian rhythm and light regulate opsin mRNA in rod photoreceptors. *Nature*, 337(6206), 454-457.

Kumar, V., & Tewary, P. D. (1983). Response to experimental photoperiods by a migratory bunting, Emberiza melanocephala. *Ibis*, 125(3), 305-312.

Kumar, V., Singh, S., Misra, M., Malik, S., & Rani, S. (2002). Role of melatonin in photoperiodic time measurement in the migratory redheaded bunting (Emberiza bruniceps) and the nonmigratory Indian weaver bird (Ploceus philippinus). *Journal of Experimental Zoology*, 292(3), 277-286.

Kumar, V., & Tewary, P. D. (1982). Photoperiodic regulation of the gonadal recrudescence in common Indian rosefinch: dependence on circadian rhythms. *Journal of Experimental Zoology*, *223*(1), 37-40.

Kumar, J., Malik, S., Bhardwaj, S. K., & Rani, S. (2021). Impact of light at night is phase dependent: A study on migratory redheaded bunting (Emberiza bruniceps). Frontiers in Ecology and Evolution, 9(1), 1-9.

Lincoln, G. A., Andersson, H., & Loudon, A. (2003). Clock genes in calendar cells as the basis of annual timekeeping in mammals--a unifying hypothesis. *The Journal of endocrinology*, *179*(1), 1-13.

Lincoln, G. (2019). A brief history of circannual time. *Journal of neuroendocrinology*, *31*(3), e12694.

MacDougall-Shackleton, S. A., Stevenson, T. J., Watts, H. E., Pereyra, M. E., & Hahn, T. P. (2009). The evolution of photoperiod response systems and seasonal GnRH plasticity in birds. *Integrative and comparative biology*, *49*(5), 580-589.

Majumdar, G., Yadav, G., Rani, S., & Kumar, V. (2014). A photoperiodic molecular response in migratory redheaded bunting exposed to a single long day. *General and comparative endocrinology*, 204, 104-113.

Majumdar, G., Rani, S., & Kumar, V. (2015). Hypothalamic gene switches control transitions between seasonal life history states in a night-migratory photoperiodic songbird. *Molecular and cellular endocrinology*, 399, 110-121.

Majumdar, G., Yadav, G., Rani, S., & Kumar, V. (2015). Bird eyes distinguish summer from winter: Retinal response to acute photoperiod change in the night-migratory redheaded bunting. *Journal of chemical neuroanatomy*, 68, 55-60.

McDonald, P. (1976). *The influence of photoperiod on male courtship and nest-building in the ring dove, Streptopelia risoria* (Doctoral dissertation, University of British Columbia).

Meier, A.H. (1981). [Review of Avian Endocrinology; Biological Rhythms in Birds, by. A. Epple, M.H. Stetson, Yuichi Tanabe, Katuhide Tamaka, & Takanori Ookawa]. The Auk, 98(4), 850-852. http://www.jstor.org/stable/4085913

Menaker, M., Roberts, R., Elliott, J., & Underwood, H. (1970). Extraretinal light perception in the sparrow, III: the eyes do not participate in photoperiodic photoreception. *Proceedings of the National Academy of Sciences*, *67*(1), 320-325.

Millam, J. R., Craig-Veit, C. B., & Farist, P. L. (1995). Concentration of chicken gonadotropin-releasing hormones I and II in microdissected areas of turkey hen brain during the reproductive cycle. *Domestic animal endocrinology*, 12(1), 1-11.

Millar, A. J. (2004). Input signals to the plant circadian clock. *Journal of Experimental Botany*, *55*(395), 277-283.

Miyamoto, K., Hasegawa, Y., Nomura, M., Igarashi, M., Kangawa, K., & Matsuo, H. (1984). Identification of the second gonadotropin-releasing hormone in chicken hypothalamus: evidence that gonadotropin secretion is probably controlled by two distinct gonadotropin-releasing hormones in avian species. *Proceedings of the National Academy of Sciences*, 81(12), 3874-3878.

Nakane, Y., Ikegami, K., Ono, H., Yamamoto, N., Yoshida, S., Hirunagi, K., ... & Yoshimura, T. (2010). A mammalian neural tissue opsin (Opsin 5) is a deep brain photoreceptor in birds. *Proceedings of the National Academy of Sciences*, 107(34), 15264-15268.

Nakane, Y., & Yoshimura, T. (2010). Deep brain photoreceptors and a seasonal signal transduction cascade in birds. *Cell and tissue research*, *342*(3), 341-344.

Nakao, N., Ono, H., Yamamura, T., Anraku, T., Takagi, T., Higashi, K., ... & Yoshimura, T. (2008). Thyrotrophin in the pars tuberalis triggers photoperiodic response. *Nature*,, 452(7185), 317-322.

Nakao, N., Yasuo, S., Nishimura, A., Yamamura, T., Watanabe, T., Anraku, T., ... & Yoshimura, T. (2007). Circadian clock gene regulation of steroidogenic acute regulatory protein gene expression in preovulatory ovarian follicles. *Endocrinology*, 148(7), 3031-3038.

Nichelmann, M., Höchel, J., & Tzschentke, B. (1999). Biological rhythms in birds—development, insights and perspectives. *Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology*, 124(4), 429-437.

Nicholls, T. J., Follett, B. K., & Robinson, J. E. (1983). A photoperiodic response in gonadectomized Japanese quail exposed to a single long day. *Journal of Endocrinology*, 97(1), 121-126.

Ohuchi, H., Yamashita, T., Tomonari, S., Fujita-Yanagibayashi, S., Sakai, K., Noji, S., & Shichida, Y. (2012). A non-mammalian type opsin 5 functions dually in the photoreceptive and non-photoreceptive organs of birds. *PloS one*, 7(2), e31534.

Onoue, T., Nishi, G., Hikima, J. I., Sakai, M., & Kono, T. (2019). Circadian oscillation of TNF-α gene expression regulated by clock gene, BMAL1 and CLOCK1, in the Japanese medaka (Oryzias latipes). *International immunopharmacology*, 70, 362-371.

Palczewski, K., Kumasaka, T., Hori, T., Behnke, C. A., Motoshima, H., Fox, B. A., ... & Miyano, M. (2000). Crystal structure of rhodopsin: AG protein-coupled receptor. *Science*s, 289(5480), 739-745.

Pérez, J. H., Tolla, E., Dunn, I. C., Meddle, S. L., & Stevenson, T. J. (2019). A comparative perspective on extra-retinal photoreception. *Trends in Endocrinology & Metabolism*, *30*(1), 39-53.

Prasad, B. N., Kumar, V., & Tewary Reader, P. D. (1982). The photo-gonadal response of a migratory bunting: Evidence of an external coincidence system. *Journal of Experimental Zoology*, 221(2), 131-135.

Raess, M., & Gwinner, E. (2005). Gonadal status upon spring arrival in long-distance and short-distance migrating stonechats (Saxicola torquata). *Journal of Ornithology*, 146(4), 325.

Rani, S., Singh, S., Misra, M., Malik, S., Singh, B. P., & Kumar, V. (2005). Daily light regulates seasonal responses in the migratory male redheaded bunting (Emberiza bruniceps). *Journal of Experimental Zoology Part A: Comparative Experimental Biology*, 303(7), 541-550.

Ravikumar, G., & Tewary, P. D. (1990). Photoperiodic control of ovarian growth in the subtropical house sparrow, Passer domesticus: evidence of an external coincidence system. *Acta biologica Hungarica*, 41(4), 333-339.

Rebay, I., Silver, S. J., & Tootle, T. L. (2005). New vision from Eyes absent: transcription factors as enzymes. *TRENDS in Genetics*, *21*(3), 163-171.

Robinson, J. E., & Follett, B. K. (1982). Photoperiodism in Japanese quail: the termination of seasonal breeding by photorefractoriness. *Proceedings of the Royal Society of London. Series B. Biological Sciences*, 215(1198), 95-116.

Saunders, D. S. (1979). External coincidence and the photoinducible phase in the Sarcophaga photoperiodic clock. *Journal of comparative physiology*, 132(2), 179-189.

Sharp, P. J. (1993). Photoperiodic control of reproduction in the domestic hen. *Poultry science*, *72*(5), 897-905.

Silverin, B., Massa, R., & Stokkan, K. A. (1993). Photoperiodic adaptation to breeding at different latitudes in great tits. *General and comparative endocrinology*, *90*(1), 14-22.

Simpson, S. M., & Follett, B. K. (1982). Formal properties of the circadian system underlying photoperiodic time-measurement in Japanese quail. *Journal of comparative physiology*, 145(3), 381-390.

Singh, O., Agarwal, N., Yadav, A., Basu, S., Malik, S., Rani, S., ... & Singru, P. S. (2020). Concurrent changes in photoperiod-induced seasonal phenotypes and hypothalamic CART peptide-containing systems in night-migratory redheaded buntings. *Brain Structure and Function*, *225*(9), 2775-2798.

Soni, B. G., & Foster, R. G. (1997). A novel and ancient vertebrate opsin. *FEBS letters*, 406(3), 279-283.

Stevenson, T. J., & Ball, G. F. (2009). Anatomical localization of the effects of reproductive state, castration, and social milieu on cells immunoreactive for gonadotropin-releasing hormone-I in male European starlings (Sturnus vulgaris). *The Journal of comparative neurology*, 517(2), 146–155.

Stevenson, T. J., & Ball, G. F. (2012). Disruption of neuropsin mRNA expression via RNA interference facilitates the photoinduced increase in thyrotropin-stimulating subunit β in birds. *European Journal of Neuroscience*, 36(6), 2859-2865.

Stevenson, T. J., & Prendergast, B. J. (2013). Reversible DNA methylation regulates seasonal photoperiodic time measurement. *Proceedings of the National Academy of Sciences*, *110*(41), 16651-16656.

Stevenson, T. J., Hahn, T. P., & Ball, G. F. (2012). Variation in Gonadotrophin-Releasing Hormone-1 Gene Expression in the Preoptic Area Predicts Transitions in Seasonal Reproductive State. *Journal of neuroendocrinology*, *24*(2), 267-274.

Stevenson, T. J., Visser, M. E., Arnold, W., Barrett, P., Biello, S., Dawson, A., ... & Helm, B. (2015). Disrupted seasonal biology impacts health, food security and ecosystems. *Proceedings of the Royal Society B: Biological Sciences*, *282*(1817), 20151453.

Stevenson, T. J., Liddle, T. A., Stewart, C., Marshall, C. J., & Majumdar, G. (2022). Neural programming of seasonal physiology in birds and mammals: A modular perspective. *Hormones and Behavior*, *142*, 105153.

Tarttelin, E. E., Bellingham, J., Hankins, M. W., Foster, R. G., & Lucas, R. J. (2003). Neuropsin (Opn5): a novel opsin identified in mammalian neural tissue. *FEBS letters*, 554(3), 410-416.

Tewary, P. D., & Kumar, V. (1982). Evidence for a circadian component in the photoperiodic mechanism of the blackheaded bunting, Emberiza melanocephala. *Animal Reproduction Science*, 5(1), 65-73.

Tewary, P. D., & Kumar, V. (1982). Photoperiodic responses of a subtropical migratory finch, the black-headed bunting (Emberiza melanocephala). *The Condor*, 84(2), 168-171.

Tewary, P. D., Prasad, B. N., & Kumar, V. (1982). Circadian basis of photoperiodically induced testicular growth in redheaded bunting, Emberiza bruniceps. *Animal Reproduction Science*, *4*(3), 245-249.

Tewary, P. D., & Prasad, B. N. (1983). Photoperiodic induction of fattening in redheaded bunting: A phenomenon of external coincidence system. *Environment Control in Biology*, 21(1), 1-5.

Tewary, P. D., & Tripathi, B. K. (1983). Photoperiodic control of reproduction in a female migratory bunting (Emberiza bruniceps). *Journal of Experimental Zoology*, 226(2), 269-272.

Tolla, E., & Stevenson, T. J. (2020). Sex differences and the neuroendocrine regulation of seasonal reproduction by supplementary environmental cues. *Integrative and Comparative Biology*, *60*(6), 1506-1516.

Turek, F. W. (1972). Circadian involvement in termination of the refractory period in two sparrows. *Science*, *178*(4065), 1112-1113.

Ueda, H. R., Hayashi, S., Chen, W., Sano, M., Machida, M., Shigeyoshi, Y., ... & Hashimoto, S. (2005). System-level identification of transcriptional circuits underlying mammalian circadian clocks. *Nature genetics*, 37(2), 187-192.

Underwood, H., Siopes, T., & Edmonds, K. (1997). Eye and gonad: role in the dual-oscillator circadian system of female Japanese quail. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, 272(1), R172-R182.

Underwood, H., & Menaker, M. (1970). Photoperiodically significant photoreception in sparrows: Is the retina involved?. *Science*, *167*(3916), 298-301.

Wada, M. (1979). Photoperiodic control of LH secretion in Japanese quail with special reference to the photoinducible phase. *General and comparative endocrinology*, *39*(2), 141-149.

Wada, Y., Okano, T., Adachi, A., Ebihara, S., & Fukada, Y. (1998). Identification of rhodopsin in the pigeon deep brain. *FEBS letters*, 424(1-2), 53-56.

Wikelski, M., Martin, L. B., Scheuerlein, A., Robinson, M. T., Robinson, N. D., Helm, B., ... & Gwinner, E. (2008). Avian circannual clocks: adaptive significance and possible involvement of energy turnover in their proximate control. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *363*(1490), 411-423.

Wood, S. H., Hindle, M. M., Mizoro, Y., Cheng, Y., Saer, B. R., Miedzinska, K., ... & Loudon, A. S. (2020). Circadian clock mechanism driving mammalian photoperiodism. *Nature communications*, *11*(1), 1-15.

Yadav, S., & Chaturvedi, C. M. (2014). Internal coincidence of serotonergic and dopaminergic oscillations modulates photo sexual responses of Japanese quail, Coturnix coturnix japonica.

Yamamura, T., Hirunagi, K., Ebihara, S., & Yoshimura, T. (2004). Seasonal morphological changes in the neuro-glial interaction between gonadotropin-releasing hormone nerve terminals and glial endfeet in Japanese quail. *Endocrinology*, 145(9), 4264-4267.

Yamamura, T., Yasuo, S., Hirunagi, K., Ebihara, S., & Yoshimura, T. (2006). T3 implantation mimics photoperiodically reduced encasement of nerve terminals by glial processes in the median eminence of Japanese quail. *Cell and tissue research*, *324*(1), 175-179.

Yamashita, T., Ohuchi, H., Tomonari, S., Ikeda, K., Sakai, K., & Shichida, Y. (2010). Opn5 is a UV-sensitive bistable pigment that couples with Gi subtype of G protein. *Proceedings of the National Academy of Sciences*, 107(51), 22084-22089.

Yasuo, S., Ebihara, S., & Yoshimura, T. (2004). Circadian expression of clock gene in the optic tectum of Japanese quail. *Brain research*, 1005(1-2), 193-196.

Yasuo, S., Watanabe, M., Okabayashi, N., Ebihara, S., & Yoshimura, T. (2003). Circadian clock genes and photoperiodism: comprehensive analysis of clock gene expression in the mediobasal hypothalamus, the suprachiasmatic nucleus, and the pineal gland of Japanese quail under various light schedules. *Endocrinology*, 144(9), 3742-3748.

Yoshimura, T., Suzuki, Y., Makino, E., Suzuki, T., Kuroiwa, A., Matsuda, Y., ... & Ebihara, S. (2000). Molecular analysis of avian circadian clock genes. *Molecular brain research*, 78(1-2), 207-215.

Yoshimura, T., Yasuo, S., Watanabe, M., Iigo, M., Yamamura, T., Hirunagi, K., & Ebihara, S. (2003). Light-induced hormone conversion of T 4 to T 3 regulates photoperiodic response of gonads in birds. *Nature*, 426(6963), 178-181.

Zamm, A., Wellman, C., & Palmer, C. (2016). Endogenous rhythms influence interpersonal synchrony. *Journal of Experimental Psychology: Human Perception and Performance*, 42(5), 611.