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Perspectives

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Seasonal timing in a changing world: the epigenetic link between environment and reproduction across taxa

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Abstract

All plants and animals must time their annual reproduction to seasonal variation in resources to optimize reproductive fitness. Environmental factors such as photoperiod and temperature are well known to influence seasonal timing of reproduction but how organisms incorporate environmental cues to alter physiological responses and initiate reproduction remains poorly characterized at the genetic level. A growing number of studies have found that epigenetic mechanisms, such as noncoding RNA, histone modification, and DNA methylation, can have an important role in modifying transcriptional regulation of traits related to seasonal timing. While epigenetic modifications act differently across taxa, there is consistent evidence for their involvement in the timing of seasonal life-history transitions. Here, we discuss the way in which environmental cues trigger epigenetic modifications and propose several roles for their involvement in the regulation of seasonal phenotypes in plants, invertebrates, and vertebrates.

Keywords **photoperiod, life-history transitions, transcription, DNA methylation, histone modification, ncRNA, circannual rhythms, epigenetics**

Introduction

Many temperate species are facing rapid environmental changes, something which has had a major impact on phenological traits such as seasonal timing of migration and reproduction [1–3]. To understand how organisms adapt to changing environmental conditions, we need a better understanding of how environmental cues are perceived and translated to modify gene expression to modify phenotypes. Phenological responses are driven to a large extent by phenotypic plasticity, [4–6] the ability of a genotype to change its phenotype in relation to environmental conditions [7]. Understanding the molecular mechanisms and evolutionary basis of phenotypic plasticity is therefore essential for predicting how populations will respond to environmental change. To advance the field requires a clearer understanding of how organisms perceive environmental cues and how such environmental cues are translated into phenotypic changes. In particular, elucidating the molecular mechanisms of environmental responsiveness in plasticity of seasonal timing should be a key priority in the years ahead.

Seasonal variation in timing of reproduction is a phenological trait that is readily observed in many different species of plants, invertebrates, and vertebrates [8]. As reproduction is costly and an important determinant of an individual's fitness, [9] reproduction is often optimized to an annual period in which resources are abundant [3,10,11]. For optimal timing of reproduction external cues are essential and phenological information is often conveyed through photoperiod in combination with cues such as temperature [12–15] (Fig. 1). While additional cues for timing, such as food abundance [10,16] and social interactions [17,18] have also been identified, it is difficult to disentangle whether the cause is due to biotic (e.g. density of prey items) or abiotic cues (e.g. prevailing phenological pattern) (Fig. 1). Importantly, differences in how organisms at different trophic levels respond to changes in environmental cues has in some cases led to a decline in synchronization of seasonal interactions among some species [19,20] some-

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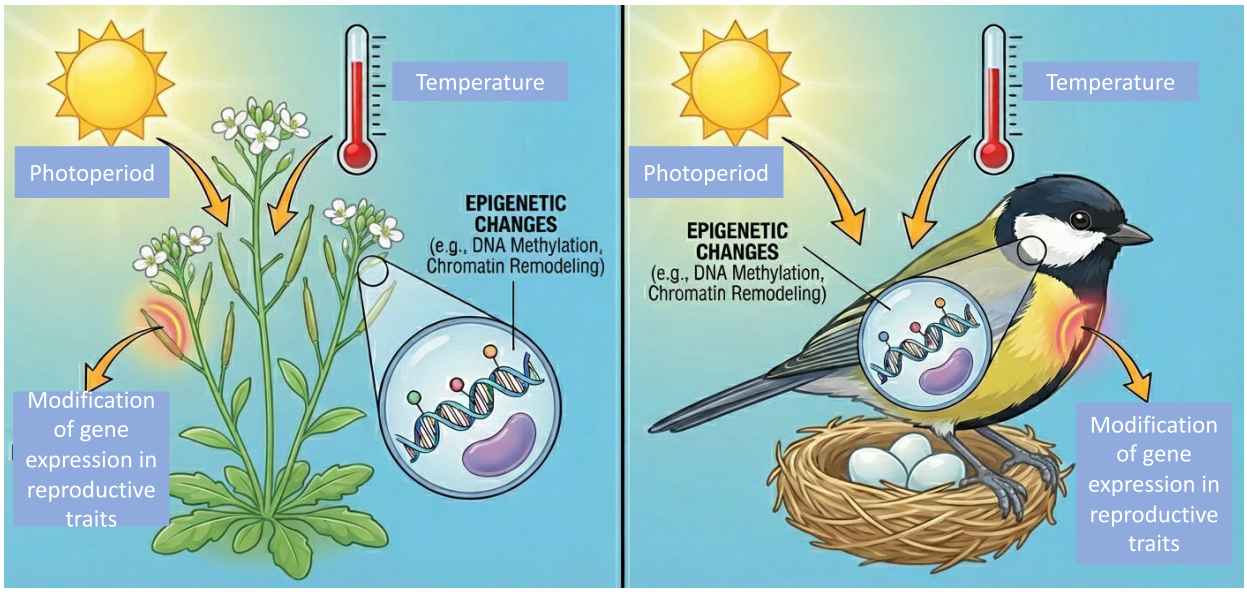

Figure 1 Phenological information from the environment leads to changes in epigenetic patterns and modulates gene expression in traits involved in seasonal timing in both plants and animals. The current gap in knowledge is in how cues are sensed and how environmentally induced changes in epigenetic patterns are transferred on in the reproductive cascade.

thing which can ultimately lead to mistiming in seasonal behaviors and reduced reproductive success [11,16,21].

To understand how organisms detect, incorporate and respond to environmental cues at a molecular level, the impact of phenological climate sensitivity needs to be resolved. Although physiologically the process of reproduction has been extensively studied, the molecular details (which genes are involved and what regulates them) are poorly understood in many species and knowledge is largely limited to model species such as *Arabidopsis thaliana*, [15] rice, [22] and the mammalian model species mice, humans, and European hamster [23,24]. Studies on these species have however revealed an important role for a set of conserved epigenetic switches in determining the onset of reproduction [25] or flowering, [15] and thus the potential role of epigenetic mechanisms for timing of seasonal rhythms has gathered increasing attention [26]. Epigenetic regulation is broadly defined as molecular modifications, which do not alter the genetic sequence *per se* but have an effect on gene expression [27]. Of the different epigenetic modifications that have been characterized so far (e.g. DNA methylation, histone modifications, and ncRNA), DNA methylation is the most studied form for several reasons: it can be modified using chemical inhibitors [28] and nucleotide level DNA methylation information can easily be obtained also in nonmodel species [29–32]. The aim of this perspective is to examine the role different epigenetic mechanisms have in seasonal timing across different taxa, from plants and insects to birds and mammals. We first briefly describe the different epigenetic mechanisms before we review the evidence for epigenetic modifications being involved in seasonal timing in different organismal groups.

Epigenetic modifications

DNA methylation is the addition, or removal, of a methyl-group predominantly at the fifth residue of cytosine in DNA and often leads to transcriptional changes depending on the gene region (e.g. promoter, TSS, and intron) [33,34] and sequence context (i.e. the combination of nucleotides next to a cytosine) [35,36]. In vertebrates, DNA methylation in gene promoters or TSS regions can have silencing effect on gene expression [37] whereas in other genomic locations (e.g. gene bodies) the effect of methylation on gene expression is more complex, although methylation in the gene body does play an important role for tissue specific expression patterns and transposable element silencing [29]. In plants, DNA methylation in non-CpG contexts occur more frequently than in vertebrates and plants also use methylation to silence transposable elements [38]. In invertebrates, DNA methylation is generally low [35] but shows considerable variation across species [39]. DNA methylation is labile and is controlled by a set of DNA methyltransferases [40] and removal of methylation marks can be either passive through repression of DNA methyltransferases [41] or active through a variety of enzymes, of which TET enzymes are most common [42].

Post-transcriptional modification of histone molecules of the nucleosome affect the compactness of chromatin and how accessible it is to transcription or the DNA repair machinery [43,44]. There are multiple different modifications, such as methylation, acetylation, phosphorylation, ubiquitinylation, sumoylation, ADP ribosylation and deamination, and the effect to transcription (activating or repressing) is dependent on the location of the modification in the histone subunit tail and in which genomic context it is [45]. DNA methylation and histone modifications often work in concert to regulate gene expression in eukaryotes [46].

Noncoding RNA molecules are also important epigenetic regulators. These are characterized based on their length from small (miRNA, pirRNA, and siRNA) to long noncoding RNA (lncRNA) [47]. Small noncoding RNA molecules are involved in chromatin modifying functions and regulation of gene expression through RNA interference whereas lncRNA usually facilitate the accumulation of chromatin modifying enzymes to specific genomic loci [48].

Epigenetic mechanisms involved in timing of flowering in plants

Transition to flowering is a major developmental switch in the plant life cycle and some of the earliest evidence that epigenetic regulation is involved came from experiments with late-flowering *Arabidopsis* and *Thlaspi* lines [49]. Burn *et al.* [49] demonstrated that treatment with a DNA demethylating agent (5-azacytidine) had the same effect for flowering as did vernalization (cold treatment), but not in plants which were unresponsive for vernalization, suggesting that vernalization released DNA methylation prevented flowering in unsuitable conditions. Subsequent work on *Arabidopsis* have demonstrated that epigenetic mechanisms play a critical role in the regulation of key flowering time genes (*FRI* and *FLC*) through chromatin modifications and long noncoding RNA [50].

The involvement of DNA methylation in flowering has also been described in other species. For example, in clonally reproducing dandelion, treatment with a cytosine (DNA) demethylating agent synchronized the clonally inherited patterns in timing of flowering between lineages [51]. Although use of DNA demethylating chemicals to generate phenotypic changes are frequently criticized for their potential side-effects [52,53] similar results linking DNA methylation to flowering time have been obtained also in experimental set-ups in nature. For example, Cortijo *et al.* [54] created isogenic *Arabidopsis* lines by crossing a recessive ddm1–2 mutation line with wild type and subsequent backcrossing of F1 to wild type and then selfing of F2. These epigenetic recombinant inbred lines (epiRILs) contained Mendelian-inherited DNA methylation differences, which explained 86.78% of the variation flowering time between isogenic lines. In *Azalea* [55], where changes in photoperiod and temperature during the rest period affected not only flowering time but also global DNA methylation patterns in flower buds across the season. These results indicate that DNA methylation as a mechanism responds to multiple environmental cues in order to time reproduction.

While much work has only considered DNA methylation there is growing support for chromatin modifications as a key mechanism in the regulation of onset of reproduction in plants (i.e. onset of cell maturation towards flowering, so-called vegetative-flowering transition). For example, the flowering locus C (FLC) system has been identified as a central core for regulation of flowering [22] and vernalization [12]. Spring photoperiod and temperatures release the repression of FLC, which opens a window for flowering gene expression. The process of vernalization is induced by prolonged periods of low temperatures and in essence reverses the histone methylation status of FLC before next year reproductive period [50]. Although the histone modifications are in response to temperature, the mechanism by which temperature sensing is mediated to alter histone modifications is still unresolved. In *Arabidopsis halleri gemmifera* levels of H3K27me3 and H3K4me3 were measured biweekly in *AhgFLC* gene for over 2 years [56]. These data showed that histone marks had differential response to temperature, such that H3K27me3 in the distal nucleation region of *AhgFLC* is responsible for its upregulated expression in spring with insensitivity to cold, whereas H3K4me3 in the same genomic region responds to cold in summer and winter when H3K27me3 is mostly absent.

Inherently linked to chromatin modifications are also lncRNA, which have been described for the *FLC* complex in *Arabidopsis*. Antisense transcript of *FLC* is strongly cold induced and participates in silencing of the *FLC* by incorporating silencing histone methylation marks in the gene region [57]. Genome-wide screens in chickpea, [58] orange, [59] and *Cajanus scarabaeoides* [60] have also characterized the potential of lncRNA to control flowering time as the molecules contain targets for flowering-related transcription factors as well as differential patterns of expression across tissues.

In conclusion, research in plants, especially rice and *Arabidopsis*, demonstrate an increasingly important role of epigenetic regulation for timing of flowering and the mechanism by which the environment modulate epigenetic changes is also starting to be understood.

Epigenetic mechanisms involved in reproduction in invertebrates

There are now many examples where epigenetic mechanisms are involved in reproductive stage transitions also in invertebrates (e.g. [61]). This is interesting because compared to vertebrates, DNA methylation levels are in general lower and methylation is mainly concentrated to gene bodies and to regions of the genome with functional importance [62]. One example of the involvement of DNA methylation in reproductive stage transitions is found in *Nasonia vitripennis*, where females exposed to short or long day light cycles showed differences in DNA methylation pattern and diapause response [63]. Using a pharmacological inhibitor to block DNA methylation as well as RNAi to knock down *DNMT1a* enzymes resulted in an abolishment of the photoperiod induced diapause response [63]. This result shows the potential of DNA methylation as a mechanism for photoperiodic response in invertebrates. Another example that DNA methylation can be an important mechanism for phenotypic variation in invertebrates is the transition between reproductive queen and nonreproductive workers in honey bee, which is determined by DNA methylation patterns in brain during development as a result of dietary differences [64]. Similarly in ants, differential DNA methylation was identified between reproductive and worker casts and at different developmental stages [65].

DNA methylation levels seem to be highly variable in insects [39] and notably near absent in some insect models such as *Drosophila* [66]. Other epigenetic mechanisms such as histone modifications and ncRNA also play an important role in many traits related to reproductive stage transitions or timing. In mosquitos (*Culex pipiens*), expression of miRNAs related to ovarian development and lipid metabolism was lower in diapause-destined females than in nondiapausing females [67]. In the European map butterfly (*Araschnia levana*) experimental manipulation of day length during metamorphosis resulted in differential expression of miRNAs between the experimental groups, which indicates that miRNA are likely involved in seasonal phenotypes, i.e. the spring or summer imagoes, in the species [68]. Also, lncRNA have been observed in *Harpegnathos* and *Camponotus* ants, and in *Harpegnathos* differential lncRNA expression was identified to be involved in caste transition from a nonreproductive worker to an egg-laying queen [69]. In eusocial insects, histone modifications have been associated with caste determination in *Camponotus floridanus* ants [70] as well as in honey bees, *Apis mellifera,* [71]. In both species, H3K27ac was associated with caste identity. In the ant, a more foraging oriented worker class, called minor, is observed along with a more protective worker class, called major. Admission of histone deacetylase inhibitor trichostatin A to eclosed major workers induced

a change in behavior to become more like foraging minors, [72] and this shift in behavior was also seen in gene expression patterns in treated major workers becoming more similar to a natural minor worker, [73] indicating that the behavior can be plastically changed via histone acetylation. In *Drosophila melanogaster* tissue specific histone methylation patterns (H3K4me3 and H3K36me1) are involved in phenotypic plasticity of reproductive diapause and thus further demonstrate how epigenetic mechanism can be important for adaptation to changing environments [74].

DNA methylation and timing of breeding in vertebrates

Breeding in vertebrates requires maturation of the reproductive tissues, which is achieved during puberty. Histone methylation is a master switch in the process of puberty and DNA methylation additionally affect genes up- and downstream of the focal region of the neuroendocrine regulators "released" by the conformation change of the histone backbone [75]. For example, in rats (*Rattus norvegicus domesticus*), pharmacological inhibition of DNMTs significantly delayed onset of puberty and more specifically genes involved with expression repressing polycomb group showed altered promoter methylation at different stages of puberty progression [75].

In many seasonally reproducing species the activation of gonads at the start of the reproductive season seems to be mainly driven by photoperiod [13,24] and recent work have found that DNA methylation can play an important role in the neuroendocrine regulation of gonadal maturation [76–78]. Seasonal variation in DNA methylation is expected [26] and has been demonstrated in a study on great tits (*Parus major*), where sampling of red blood cells from the same females over the course of 5 months during the breeding season found that nearly 10% of analysed CpG sites exhibited significant variation [32]. When this seasonal variation in methylation was anchored to the laying of the first egg, most variation in red blood cell DNA methylation was found between the prelaying and postlaying stages within a few candidate genes [including *NR5A1* and *LOC107215054* (*MYLK*-like)] known to be involved in oviposition-ing [79]. In the Siberian hamster (*Phodopus sungorus*), day length is transmitted through melatonin levels and subsequently indirectly regulates *de novo* DNA methyltransferase expression [76]. Current evidence indicates that higher estrogen levels in long photoperiod conditions induces hypothalamic *Dnmt* expression, [78] whereas triiodothyronine have little to no impact [80]. Long photoperiod increases in Dnmt expression are associated with elevated DNA methylation at the promoter region of *DIO3* within the hypothalamus, which may facilitate reduced *DIO3* expression and activation of a breeding state.

A recent study in great tits also link hormonal levels to epigenetic changes as the authors found that manipulation of female hormone levels (yolk testosterone) caused sex-specific changes in DNA methylation levels at over 700 sites, many in genes associated with growth and reproduction [81]. Effects on global DNA methylation patterns in response to manipulation of corticostrone in zebra finches has also been observed, [82] further highlighting interaction between hormonal regulation and epigenetic modifications.

Involvement of photoperiod on chromatin modifications has also been reported in the gonads of the Siberian hamster [83]. Males exposed to short day length exhibited increased levels of histone deacetylase *HDAC3*, which together with increased *Dnmt3a* expression [76] are involved in the regulation of seasonal changes in gonadal function, such as gametogenesis and/or steroidogenesis. In females no increase in ovarian *HDAC* expression was observed in response to day length but in uterus short day lengths increased *HDAC 2* expression as a response to decreased ovarian steroid levels [83]. Taken together, these data highlight dynamic changes in enzymes linked to epigenetic modifications and that associated molecular changes occur across the hypothalamo–gonadal axis.

How do environment signals lead to epigenetic modification?

As the above demonstrates, there are several studies across a wide range of taxa that illustrate a role for epigenetic mechanisms to regulate seasonal timing of reproduction. The key questions is how such epigenetic modifications are altered by seasonal environmental cues?

Temperature, for example, alters histone methylation patterns in the promotor of the BDNF gene in the hypothalamus in chickens (*Gallus gallus*) exposed to temperature treatment at early age [84] and in guinea pigs (*Cavia aperea*), temperature exposure of the father resulted in DNA methylation differences in liver tissue between offspring sired prior to and after exposure (an example of transgenerational effect of methylation) [85]. Other abiotic environmental conditions can also affect methylation through stress response and the glucocorticoid pathway. In the superb starling (*Lamprotornis superbus*) a positive correlation between prebreeding rainfall and DNA methylation levels in the glucocorticoid receptor promoter region of 1-week-old chicks was observed and it also affected breeding success of males in adulthood [86]. In rice, cultivar-specific hypo- and hypermethylation patterns were measured after experimental exposure to drought and salinity stress [87]. The cultivars which differed in regard to their tolerance to drought or salinity also contained cytosine mutations affecting methylation patterns in genes responsive to the stress treatment. In honeybee (*A. mellifera*) the social context, namely presence or absence of young adults or brood, affect the expression and proportions of DNA methyltransferases over time highlighting the potential for epigenetic regulation of the casts and social tasks in the colony [88]. In the ant *Temnothorax longispinosus*, histone acetylation is involved in regulation of circadian rhythms, [89] in a similar manner to other organisms [26]. In *A. thaliana*, the vernalization process is affected by multiple temperature sensing inputs to be used to finetune flowering to spring and interact with the FLC locus [90].

As the above examples demonstrate, there are a variety of environmental factors that can alter epigenetic marks—the question is how do these different environmental sources modify the different epigenetic mechanisms.

All plants and animals have specific photoreceptors that sense light and the photoreceptors interact with different transcription factors, for example the phytochrome interacting factors (PIFs) in plants, who integrate external signals such as photoperiod to control downstream gene regulation [91]. *Arabidopsis*, for example, have several PIFs that interact with different photoreceptors as well as with transcription factors to alter histone and methylation patterns, both at specific genes as well as by large-scale genome reorganization.

Taken together, these studies exemplify that both biotic and abiotic factors can be conveyed to alter epigenetic patterns and that the mechanism by which this occur is starting to be elucidated.

Future directions

If we are to understand how organisms may adapt to changing environmental conditions, we need studies that bridge the current gap of how environmental cues modify epigenetic change and leads to changes in epigeneic gene expression in the relevant tissues that initiate seasonal timing of reproduction (Fig. 1). There are now many studies that correlate epigenetic changes to seasonal timing of reproduction across a wide range of taxa, leaving little doubt that epigenetic mechanisms are involved. What is not yet well understood is the molecular mechanism by which environmental factors lead to these epigenetic changes and how epigenetic changes in turn alters gene activity and we see this is an area of research that needs urgent attention.

An important caveat with many current studies is the lack of functional assays to verify the involvement of the different epigenetic modifications as they rely on correlation between DNA methylation status, ncRNA, and histone modification patterns and the phenotype [32,49 ,55,63,79,86]. While this is not a specific criticism against epigenetic studies and applies equally well to genome-wide association studies or gene expression studies, given the high interest and scrutiny of epigenetic studies functional verification seems particularly prudent in this field [92, 98].

The question in the field is thus no longer whether epigenetic mechanisms are involved but rather how they are modulated by environmental factors. We therefore urgently need better insight into how environmental information is perceived and transferred to the epigenetic machinery and how it ultimately modulates gene expression patterns. There is no doubt that external cues can affect essential reproductive genes through epigenetic changes, [76], and it is important to understand how such changes across time participate in creating plasticity in seasonal timing. The ideal way to identify temporal patterns of DNA methylation would be to examine tissues relevant for reproduction along the time axis of maturation and reproduction, and relate the observed methylation changes to transcriptomic changes. However, at least in animals this is difficult as sampling of relevant tissues repeatedly and noninvasively is often not feasible [23] and, instead, secondary tissue types are often used (e.g. blood [93]). Moreover, there are sex-differences in how environmental cues are perceived to time reproduction, [94,95] which together with emerging evidence that DNA methylation is pivotal for the establishment of sex differences in the brain, [96] suggest that environmental cues may impact male and female epigenetic patterns differently with implications for our understanding of seasonal timing and its inheritance. While DNA methylation is currently the easiest epigenetic mechanism to examine in emerging model species other epigenetic mechanisms, such as histone modification and ncRNAs are equally important regulators in model species [56,97] and in crop plants [58,59]. We therefore expect that as it becomes more feasible to study different types of epigenetic modifications in an evolutionary ecology context a deeper role for epigenetic modifications in regulation of seasonal timing will surely emerge. Understanding how such epigenetic mechanisms are controlled by external cues to modulate phenotypes will provide valuable insights into how species can adapt to rapidly changing environments.

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Author contributions

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Conflicts of interest

The authors declare that they have no competing interests.

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References

1. Root TL, Price JT, Hall KR. *et al.* Fingerprints of global warming on wild animals and plants. *Nature* 2003;**421**:57–60. https://doi.org/10.1038/nature01333
2. Hällfors MH, Antão LH, Itter M. *et al.* Shifts in timing and duration of breeding for 73 boreal bird species over four decades. *Proc Natl Acad Sci* 2020;**117**:18557–65. https://doi.org/10.1073/pnas.1913579117
3. Cook BI, Wolkovich EM, Parmesan C. Divergent responses to spring and winter warming drive community level flowering trends. *Proc Natl Acad Sci* 2012;**109**:9000–9005. https://doi.org/10.1073/pnas.1118364109
4. Biquet J, Bonamour S, de Villemereuil P. *et al.* Phenotypic plasticity drives phenological changes in a Mediterranean blue tit population. *J Evol Biol* 2022;**35**:347–59. https://doi.org/10.1111/jeb.13950
5. Charmantier A, Gienapp P. Climate change and timing of avian breeding and migration: evolutionary versus plastic changes. *Evol Appl* 2014;**7**:15–28. https://doi.org/10.1111/eva.12126
6. Ramirez-Parada TH, Park IW, Record S. *et al.* Plasticity and not adaptation is the primary source of temperature-mediated variation in flowering phenology in North America. *Nat Ecol Evol* 2024;**8**:467–76. https://doi.org/10.1038/s41559-023-02304-5
7. Fox RJ, Donelson JM, Schunter C. *et al.* Beyond buying time: the role of plasticity in phenotypic adaptation to rapid environmental change. *Philos Trans R Soc B Biol Sci* 2019;**374**:20180174. https://doi.org/10.1098/rstb.2018.0174
8. Helm B, Ben-Shlomo R, Sheriff MJ. *et al.* Annual rhythms that underlie phenology: biological time-keeping meets environmental change. *Proc R Soc B Biol Sci* 2013;**280**:20130016. https://doi.org/10.1098/rspb.2013.0016

9. Zera AJ, Harshman LG. The physiology of life history trade-offs in animals. *Annu Rev Ecol Syst* 2001;**32**:95–126. https://doi.org/10.1146/annurev.ecolsys.32.081501.114006
10. Visser ME, Holleman LJM, Gienapp P. Shifts in caterpillar biomass phenology due to climate change and its impact on the breeding biology of an insectivorous bird. *Oecologia* 2006;**147**:164–72. https://doi.org/10.1007/s00442-005-0299-6
11. Plard F, Gaillard J-M, Coulson T. *et al.* Mismatch between birth date and vegetation phenology slows the demography of roe deer. *PLoS Biol* 2014;**12**:1–8. https://doi.org/10.1371/journal.pbio.1001828
12. Shindo C, Lister C, Crevillen P. *et al.* Variation in the epigenetic silencing of FLC contributes to natural variation in *Arabidopsis* vernalization response. *Genes Dev* 2006;**20**:3079–83. https://doi.org/10.1101/gad.405306
13. Perfito N, Jeong SY, Silverin B *et al.* Anticipating spring: wild populations of great tits (*Parus major*) differ in expression of key genes for photoperiodic time measurement. *PLoS One* 2012;**7**. https://doi.org/10.1371/journal.pone.0034997
14. te Marvelde L, Schaper SV, Visser ME. A single long day triggers follicle growth in captive female great tits (*Parus major*) in winter but does not affect laying dates in the wild in spring. *PLoS One* 2012;**7**. https://doi.org/10.1371/journal.pone.0035617
15. Andrés F, Coupland G. The genetic basis of flowering responses to seasonal cues. *Nat Rev Genet* 2012;**13**:627–39.
16. Hegland SJ, Nielsen A, Lázaro A. *et al.* How does climate warming affect plant-pollinator interactions? *Ecol Lett* 2009;**12**:184–95. https://doi.org/10.1111/j.1461-0248.2008.01269.x
17. Waas JR, Colgan PW, Boag PT. Playback of colony sound alters the breeding schedule and clutch size in zebra finch (*Taeniopygia guttata*) colonies. *Proc R Soc B Biol Sci* 2005;**272**:383–88. https://doi.org/10.1098/rspb.2004.2949
18. Dufty AM, Wingfield JC. The influence of social cues on the reproductive endocrinology of male brown-headed cowbirds: field and laboratory studies. *Horm Behav* 1986;**20**:222–34. https://doi.org/10.1016/0018-506X(86)90020-6
19. Thackeray SJ, Henrys PA, Hemming D *et al.* Phenological sensitivity to climate across taxa and trophic levels. *Nature* 2016;**535**:241–45. https://doi.org/10.1038/nature18608
20. Rehnus M, Peláez M, Bollmann K. Advancing plant phenology causes an increasing trophic mismatch in an income breeder across a wide elevational range. *Ecosphere* 2020;**11**. https://doi.org/10.1002/ecs2.3144
21. Ramírez F. *et al.* Oceanographic drivers and mistiming processes shape breeding success in a seabird. *Proc R Soc B Biol Sci* 2016;**283**:20152287.
22. Jeong HJ, Yang J, Yi J. *et al.* Controlling flowering time by histone methylation and acetylation in *Arabidopsis* and rice. *J Plant Biol* 2015;**58**:203–10. https://doi.org/10.1007/s12374-015-0219-1
23. Rzeczkowska PA, Hou H, Wilson MD. *et al.* Epigenetics: a new player in the regulation of mammalian puberty. *Neuroendocrinology* 2014;**99**:139–55. https://doi.org/10.1159/000362559
24. Sáenz de Miera C. *et al.* A circannual clock drives expression of genes central for seasonal reproduction. *Curr Biol* 2014;**24**:1500–1506. https://doi.org/10.1016/j.cub.2014.05.024
25. Kelly T, Trasler J. Reproductive epigenetics. *Clin Genet* 2004;**5**:247–60. https://doi.org/10.1111/j.0009-9163.2004.00236.x
26. Stevenson TJ. Epigenetic regulation of biological rhythms: an evolutionary ancient molecular timer. *Trends Genet* 2018;**34**:90–100. https://doi.org/10.1016/j.tig.2017.11.003
27. Allis CD, Jenuwein T. The molecular hallmarks of epigenetic control. *Nat Rev Genet* 2016;**17**:487–500. https://doi.org/10.1038/nrg.2016.59
28. Goffin J, Eisenhauer E. DNA methyltransferase inhibitors—state of the art. *Ann Oncol* 2002;**13**:1699–716at https://doi.org/10.1093/annonc/mdf314
29. Derks MFL, Schachtschneider KM, Madsen O *et al.* Gene and transposable element methylation in great tit (*Parus major*) brain and blood. *BMC Genomics* 2016;**17**:332. https://doi.org/10.1186/s12864-016-2653-y
30. Su C, Wang C, He L. *et al.* Shotgun bisulfite sequencing of the *Betula platyphylla* genome reveals the tree's DNA methylation patterning. *Int J Mol Sci* 2014;**15**:22874–86. https://doi.org/10.3390/ijms151222874
31. Libbrecht R, Oxley PR, Keller L. *et al.* Robust DNA methylation in the clonal raider ant brain. *Curr Biol* 2016;**26**:391–95. https://doi.org/10.1016/j.cub.2015.12.040
32. Viitaniemi HM, Verhagen I, Visser ME *et al.* Seasonal variation in genome-wide DNA methylation patterns and the onset of seasonal timing of reproduction in great tits. *Genome Biol Evol* 2019;**11**:970–83. https://doi.org/10.1093/gbe/evz044
33. Klose RJ, Bird AP. Genomic DNA methylation: the mark and its mediators. *Trends Biochem Sci* 2006;**31**:89–97. https://doi.org/10.1016/j.tibs.2005.12.008
34. Jones PA. Functions of DNA methylation: islands, start sites, gene bodies and beyond. *Nat Rev Genet* 2012;**13**:484–92. https://doi.org/10.1038/nrg3230
35. Suzuki MM, Bird A. DNA methylation landscapes: provocative insights from epigenomics. *Nat Rev Genet* 2008;**9**:465–76. https://doi.org/10.1038/nrg2341
36. Niederhuth CE, Bewick AJ, Ji L *et al.* Widespread natural variation of DNA methylation within angiosperms. *Genome Biol* 2016;**17**:194. https://doi.org/10.1186/s13059-016-1059-0
37. Deaton A, Bird A. CpG islands and the regulation of transcription. *Genes Dev* 2011;**25**:1010–22. https://doi.org/10.1101/gad.2037511
38. Chan SWL, Henderson IR, Jacobsen SE. Gardening the genome: DNA methylation in *Arabidopsis thaliana*. *Nat Rev Genet* 2005;**6**:351–60. https://doi.org/10.1038/nrg1601
39. Bewick AJ, Vogel KJ, Moore AJ. *et al.* Evolution of DNA methylation across insects. *Mol Biol Evol* 2017;**34**:654–65.
40. Jaenisch R, Bird A. Epigenetic regulation of gene expression: how the genome integrates intrinsic and environmental signals. *Nat Genet* 2003;**33**:245–54. https://doi.org/10.1038/ng1089
41. Law JA, Jacobsen SE. Establishing, maintaining and modifying DNA methylation patterns in plants and animals. *Nat Rev Genet* 2010;**11**:204–20. https://doi.org/10.1038/nrg2719
42. Wu SC, Zhang Y. Active DNA demethylation: many roads lead to Rome. *Nat Rev Mol Cell Biol* 2010;**11**:607–20. https://doi.org/10.1038/nrm2950
43. Lawrence M, Daujat S, Schneider R. Lateral thinking: how histone modifications regulate gene expression. *Trends Genet* 2016;**32**:42–56. https://doi.org/10.1016/j.tig.2015.10.007
44. Cosgrove MS, Boeke JD, Wolberger C. Regulated nucleosome mobility and the histone code. *Nat Struct Mol Biol* 2004;**11**:1037–43. https://doi.org/10.1038/nsmb851
45. Kouzarides T. Chromatin modifications and their function. *Cell* 2007;**128**:693–705. https://doi.org/10.1016/j.cell.2007.02.005
46. Du J, Johnson LM, Jacobsen SE. *et al.* DNA methylation pathways and their crosstalk with histone methylation. *Nat Rev Mol Cell Biol* 2015;**16**:519–32. https://doi.org/10.1038/nrm4043
47. Chhabra R. The epigenetics of noncoding-RNA. In: Tollefsbol TO (ed.), *Handbook of Epigenetics: The New Molecular and Medical Genetics*. London: Academic Press, 2022, 55–68.

48. Mangiavacchi A, Morelli G, Orlando V. Behind the scenes: how RNA orchestrates the epigenetic regulation of gene expression. *Front Cell Dev Biol* 2023;**11**:1–13. https://doi.org/10.3389/fcell.2023.1123975
49. Burn JE, Bagnall DJ, Metzger JD. *et al.* DNA methylation, vernalization, and the initiation of flowering. *Proc Natl Acad Sci USA* 1993;**90**:287–91. https://doi.org/10.1073/pnas.90.1.287
50. Berry S, Dean C. Environmental perception and epigenetic memory: mechanistic insight through FLC. *Plant J* 2015;**83**:133–48. https://doi.org/10.1111/tpj.12869
51. Wilschut RA, Oplaat C, Snoek LB. *et al.* Natural epigenetic variation contributes to heritable flowering divergence in a widespread asexual dandelion lineage. *Mol Ecol* 2016;**25**:1759–68. https://doi.org/10.1111/mec.13502
52. Griffin PT, Niederhuth CE, Schmitz RJ. A comparative analysis of 5-azacytidine-and zebularine-induced DNA demethylation. *G3 Genes Genomes Genet* 2016;**6**:2773–80. https://doi.org/10.1534/g3.116.030262
53. Ellers J, Visser M, Mariën J. *et al.* The importance of validating the demethylating effect of 5-aza-2′-deoxycytidine in model species: (A comment on cook, "DNA methylation and sex allocation in the parasitoid wasp *Nasonia vitripennis*"). *Am Nat* 2019;**194**:422–31. https://doi.org/10.1086/704247
54. Cortijo S,Wardenaar,Colomé-Tatché., *et al.* Mapping the epigenetic basis of complex traits. *Science* 2014;**343**:1145–48. https://doi.org/10.1126/science.1248127
55. Meijón M, Feito I, Valledor L. *et al.* Promotion of flowering in azaleas by manipulating photoperiod and temperature induces epigenetic alterations during floral transition. *Physiol Plant* 2011;**143**:82–92.
56. Nishio H, Buzas DM, Nagano AJ. *et al.* Repressive chromatin modification underpins the long-term expression trend of a perennial flowering gene in nature. *Nat Commun* 2020;**11**. https://doi.org/10.1038/s41467-020-15896-4
57. Swiezewski S, Liu F, Magusin A. *et al.* Cold-induced silencing by long antisense transcripts of an *Arabidopsis* Polycomb target. *Nature* 2009;**462**:799–802. https://doi.org/10.1038/nature08618
58. Khemka N, Singh VK, Garg R. *et al.* Genome-wide analysis of long intergenic non-coding RNAs in chickpea and their potential role in flower development. *Sci Rep* 2016;**6**:33297. https://doi.org/10.1038/srep33297
59. Wang C-Y, Liu S-R, Zhang X-Y *et al.* Genome-wide screening and characterization of long non-coding RNAs involved in flowering development of trifoliate orange (*Poncirus trifoliata* L. Raf.). *Sci Rep* 2017;**7**:43226. https://doi.org/10.1038/srep43226
60. Das A, Saxena S, Kumar K *et al.* Non-coding RNAs having strong positive interaction with mRNAs reveal their regulatory nature during flowering in a wild relative of pigeonpea (*Cajanus scarabaeoides*). *Mol Biol Rep* 2020;**47**:3305–17. https://doi.org/10.1007/s11033-020-05400-y
61. Maleszka R. Epigenetic integration of environmental and genomic signals in honey bees. The critical interplay of nutritional, brain and reproductive networks. *Epigenetics* 2008;**3**:188–92. https://doi.org/10.4161/epi.3.4.6697
62. Keller TE, Han P, Yi SV. Evolutionary transition of promoter and gene body DNA methylation across invertebrate-vertebrate boundary. *Mol Biol Evol* 2016;**33**:1019–28. https://doi.org/10.1093/molbev/msv345
63. Pegoraro M, Bafna A, Davies NJ. *et al.* DNA methylation changes induced by long and short photoperiods in *Nasonia*. *Genome Res* 2016;**26**:203–10. https://doi.org/10.1101/gr.196204.115
64. Lyko F, Foret S, Kucharski R *et al.* The honey bee epigenomes: differential methylation of brain DNA in queens and workers. *PLoS Biol* 2010;**8**. https://doi.org/10.1371/journal.pbio.1000506
65. Morandin C, Brendel VP, Sundström L. *et al.* Changes in gene DNA methylation and expression networks accompany caste specialization and age-related physiological changes in a social insect. *Mol Ecol* 2019;**28**:1975–93. https://doi.org/10.1111/mec.15062
66. Saravanan KA, Kumar H, Chhotaray S *et al. Drosophila melanogaster*: a promising model system for epigenetic research. *Biol Rhythm Res* 2019;**53**:1–19. https://doi.org/10.1080/09291016.2019.1685216
67. Meuti ME, Bautista-Jimenez R, Reynolds JA. Evidence that microRNAs are part of the molecular toolkit regulating adult reproductive diapause in the mosquito, *Culex pipiens*. *PLoS One* 2018;**13**. https://doi.org/10.1371/journal.pone.0203015
68. Mukherjee K, Baudach A, Vogel H. *et al.* Seasonal phenotype-specific expression of microRNAs during metamorphosis in the European map butterfly *Araschnia levana*. *Arch Insect Biochem Physiol* 2020;**104**:21657. https://doi.org/10.1002/arch.21657
69. Shields EJ, Sheng L, Weiner AK. *et al.* High-quality genome assemblies reveal long non-coding RNAs expressed in ant brains. *Cell Rep* 2018;**23**:3078–90. https://doi.org/10.1016/j.celrep.2018.05.014
70. Simola DF, Ye C, Mutti NS. *et al.* A chromatin link to caste identity in the carpenter ant *Camponotus floridanus*. *Genome Res* 2013;**23**:486–96. https://doi.org/10.1101/gr.148361.112
71. Wojciechowski M, Lowe R, Maleszka J *et al.* Phenotypically distinct female castes in honey bees are defined by alternative chromatin states during larval development. *Genome Res* 2018;**28**:1532–42. https://doi.org/10.1101/gr.236497.118
72. Simola DF, Graham RJ, Brady CM. *et al.* Epigenetic (re)programming of caste-specific behavior in the ant *Camponotus floridanus*. *Science* 2016;**351**. https://doi.org/10.1126/science.aac6633
73. Glastad KM, Graham RJ, Ju L *et al.* Epigenetic regulator CoREST controls social behavior in ants. *Mol Cell* 2020;**77**:338–351.e6. https://doi.org/10.1016/j.molcel.2019.10.012
74. DiVito Evans A, Fairbanks RA, Schmidt P. *et al.* Histone methylation regulates reproductive diapause in *Drosophila melanogaster*. *PLoS Genet* 2023;**19**:1–28. https://doi.org/10.1371/journal.pgen.1010906
75. Lomniczi A, Loche A, Castellano JM *et al.* Epigenetic control of female puberty. *Nat Neurosci* 2013;**16**:281–89. https://doi.org/10.1038/nn.3319
76. Stevenson TJ, Prendergast BJ. Reversible DNA methylation regulates seasonal photoperiodic time measurement. *Proc Natl Acad Sci USA* 2013;**110**:16651–56. https://doi.org/10.1073/pnas.1310643110
77. Lynch EWJ, Coyle CS, Lorgen M *et al.* Cyclical DNA methyltransferase 3a expression is a seasonal and estrus timer in reproductive tissues. *Endocrinology* 2016;**157**:2469–78. https://doi.org/10.1210/en.2015-1988
78. Coyle CS, Caso F, Tolla E *et al.* Ovarian hormones induce de novo DNA methyltransferase expression in the Siberian hamster suprachiasmatic nucleus. *J Neuroendocrinol.* 2020;**32**. https://doi.org/10.1111/jne.12819
79. Lindner M, Laine VN, Verhagen I *et al.* Rapid changes in DNA methylation associated with the initiation of reproduction in a small songbird. *Mol Ecol* 2021;**30**:3645–59. https://doi.org/10.1111/mec.15803
80. Tolla E, Stevenson TJ. Photoperiod-induced changes in hypothalamic de novo DNA methyltransferase expression are independent of triiodothyronine in female Siberian hamsters (*Phodopus sungorus*). *Gen Comp Endocrinol* 2020;**299**:113604. https://doi.org/10.1016/j.ygcen.2020.113604
81. Sepers B, Ruuskanen S, van Mastrigt T. *et al.* DNA methylation associates with sex-specific effects of experimentally increased yolk

testosterone in wild nestlings. *Mol Ecol* 2025;**34**:1–14. https://doi.org/10.1111/mec.17647
82. Miltiadous A, Callahan DL, Dujon AM. *et al.* Maternally derived avian corticosterone affects offspring genome-wide DNA methylation in a passerine species. *Mol Ecol* 2024;**33**:1–11. https://doi.org/10.1111/mec.17283
83. Lynch EWJ, Coyle CS, Stevenson TJ. Photoperiodic and ovarian steroid regulation of histone deacetylase 1, 2, and 3 in Siberian hamster (*Phodopus sungorus*) reproductive tissues. *Gen Comp Endocrinol* 2017;**246**:194–99. https://doi.org/10.1016/j.ygcen.2016.12.008
84. Kisliouk T, Meiri N. A critical role for dynamic changes in histone H3 methylation at the Bdnf promoter during postnatal thermotolerance acquisition. *Eur J Neurosci* 2009;**30**:1909–22. https://doi.org/10.1111/j.1460-9568.2009.06957.x
85. Weyrich A, Lenz D, Jeschek M *et al.* Paternal intergenerational epigenetic response to heat exposure in male Wild Guinea pigs. *Mol Ecol* 2016;**25**:1729–40. https://doi.org/10.1111/mec.13494
86. Rubenstein DR, Skolnik H, Berrio A *et al.* Sex-specific fitness effects of unpredictable early life conditions are associated with DNA methylation in the avian glucocorticoid receptor. *Mol Ecol* 2016;**25**:1714–28. https://doi.org/10.1111/mec.13483
87. Rajkumar MS, Shankar R, Garg R. *et al.* Bisulphite sequencing reveals dynamic DNA methylation under desiccation and salinity stresses in rice cultivars. *Genomics* 2020;**112**:3537–48. https://doi.org/10.1016/j.ygeno.2020.04.005
88. Cardoso-Júnior CAM, Eyer M, Dainat B. *et al.* Social context influences the expression of DNA methyltransferase genes in the honeybee. *Sci Rep* 2018;**8**:1–7.
89. Libbrecht R, Nadrau D, Foitzik S. A role of histone acetylation in the regulation of circadian rhythm in ants. *iScience* 2020;**23**. https://doi.org/10.1016/j.isci.2020.100846
90. Antoniou-Kourounioti RL, Hepworth J, Heckmann A *et al.* Temperature sensing is distributed throughout the regulatory network that controls FLC epigenetic silencing in vernalization. *Cell Syst* 2018;**7**:643–655.e9. https://doi.org/10.1016/j.cels.2018.10.011
91. Perrella G, Zioutopoulou A, Headland LR. *et al.* The impact of light and temperature on chromatin organization and plant adaptation. *J Exp Bot* 2020;**71**:5247–55. https://doi.org/10.1093/jxb/eraa154
92. Gudmunds E, Wheat CW, Khila A. *et al.* Functional genomic tools for emerging model species. *Trends Ecol Evol* 2022;**37**:1104–15. https://doi.org/10.1016/j.tree.2022.07.004
93. Husby A. On the use of blood samples for measuring DNA methylation in ecological epigenetic studies. *Integr Comp Biol* 2020;**60**:1558–66. https://doi.org/10.1093/icb/icaa123
94. Ball GF, Ketterson ED. Sex differences in the response to environmental cues regulating seasonal reproduction in birds. *Philos Trans R Soc B Biol Sci* 2008;**363**:231–46. https://doi.org/10.1098/rstb.2007.2137
95. Tolla E, Stevenson TJ. Sex differences and the neuroendocrine regulation of seasonal reproduction by supplementary environmental cues. *Integr Comp Biol* 2020;**60**:1506–16. https://doi.org/10.1093/icb/icaa096
96. McCarthy MM, Nugent BM. At the frontier of epigenetics of brain sex differences. *Front Behav Neurosci* 2015;**9**. https://doi.org/10.3389/fnbeh.2015.00221
97. Lomniczi A, Wright H, Ojeda SR. Epigenetic regulation of female puberty. *Front Neuroendocrinol* 2015;**36**:90–107. https://doi.org/10.1016/j.yfrne.2014.08.003
98 ,Husby A. "Wild Epigenetics: Insights from Epigenetic Studies on Natural Populations." *Proc Biol Sci*. 2022;**289**:1968. https://doi.org/10.1098/rspb.2021.1633.

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