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Epigenetic Regulation Can Function as Context Memory Linking Developmental Plasticity with Transgenerational Environmental Effects in Insects

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ABSTRACT

Insect epigenetics is often discussed as though developmental plasticity, persistent molecular state, parental effects and transgenerational inheritance formed a single continuum. They do not. This molecular perspective argues that a more useful interpretation is to separate immediate regulatory responses from epigenetic states that persist across developmental transitions, and to separate both from germline transmission. Across insects, chromatin accessibility, DNA methylation, histone modification and noncoding RNA differ markedly in taxonomic distribution, developmental timing, tissue specificity and causal support. Drosophila studies resolve chromatin accessibility into pioneering and enhancer-activation steps, honeybee caste studies reveal alternative developmental chromatin and histone states, and recent methylation work shows both functional involvement and clear null or reset cases. Histone perturbation provides stronger causal evidence for diapause regulation than most methylation studies, whereas noncoding RNAs illustrate regulatory potency without, by themselves, establishing inherited environmental information. We therefore introduce context memory as a proposed interpretive category: an epigenetically associated state that outlasts its initiating developmental or environmental context sufficiently to bias a later state or response, without presuming meiotic inheritance. The framework is intentionally mechanism-specific and evidence-bounded, and it reserves transgenerational inheritance for cases that satisfy stricter generational and causal criteria.

Keywords: Chromatin accessibility, DNA methylation, Histone modification, Noncoding RNA, Developmental plasticity, Transgenerational epigenetic inheritance

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Introduction

Insect epigenetics encompasses diverse regulatory systems rather than a conserved molecular program [1]. That diversity matters because developmental plasticity can be associated with chromatin, methylation, histone or RNA changes without those changes having the same persistence, causal status or evolutionary meaning [2]. A major interpretive problem is therefore not whether an epigenetic signal is present, but what biological interval it spans: immediate response, persistence through cell divisions or developmental transitions, effects on descendants, or stable germline transmission.

Mechanistic inference must remain stricter than molecular association. Correlated epigenomic profiles can identify candidate regulatory states, but they do not by themselves establish the carrier, direction or duration of a

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biological effect [3]. The same caution applies across generations. Transgenerational epigenetic inheritance requires exposure-generation logic and mechanism-aware separation from direct exposure, parental physiology and genetic inheritance [4, 5]. This perspective therefore proposes context memory as an intermediate analytical category, not an established mechanism: a molecularly associated state that persists beyond the initiating context long enough to bias a later state or response, while remaining agnostic about meiotic transmission. The following sections ask which insect epigenetic mechanisms can satisfy progressively stronger parts of that definition and where the evidence stops.

Results and Discussion

Chromatin accessibility is useful for this problem because it can represent a structured regulatory state without being equivalent to transcriptional output or inheritance. Comparative Drosophila work shows that accessibility has locus- and genotype-dependent robustness and evolutionary structure [6]. In early Drosophila embryos, accessibility establishment can also be mechanistically decomposed: Zelda provides pioneering accessibility, whereas patterning transcription factors augment accessibility in activation-permissive contexts [7]. This distinction separates state establishment from downstream regulatory use, a separation that any memory claim must preserve.

Accessibility also constrains, rather than simply activates, developmental response. Mutational enhancer libraries show that enhancer architecture and chromatin context delimit the expression phenotypes accessible to sequence variation [8]. Conversely, increased accessibility can facilitate repression when the relevant cis-regulatory context contains repressor logic, as shown for a Drosophila pigmentation silencer [9]. Open chromatin therefore cannot be treated as a directional proxy for "activation" or for environmental memory.

Honey-bee caste development extends the problem from enhancer logic to organismal plasticity. Multiomic and chromatin-state studies show progressively diverging queen- and worker-associated epigenomic states during larval development [10, 11]. These data support persistent developmental organization, but not germline inheritance. A 2025 reciprocal-cross study adds a further mechanistic boundary: parent-of-origin transcription in caste development was associated with histone-state differences, while DNA methylation did not account for the parent-of-origin pattern [12]. Thus, even within one plastic phenotype, distinct epigenetic layers are not interchangeable.

DNA methylation where relevant

DNA methylation must be treated as a lineage-specific mechanism rather than the default definition of insect epigenetics. Comparative methylomes show pronounced variation among insect lineages, including reductions or losses of methylation machinery, and do not support a universal association between methylation and sociality [13]. This evolutionary heterogeneity makes "where relevant" a mechanistic requirement: methylation evidence should be interpreted only in taxa, tissues and stages in which the machinery and mark are demonstrably informative.

Developmental studies further show that methylation can be rewritten. In *Bombus terrestris*, methylation patterns differ across sex, tissue and developmental context in a manner consistent with female-specific developmental erasure in the studied system [14]. In *Helicoverpa armigera*, non-CG methylation changes mark the pupal-to-adult transition [15]. Neither result establishes causal control of metamorphosis or a retained memory state; both instead show that major developmental transitions can alter the methylation landscape that a persistence claim would need to track.

Functional evidence is also context dependent. DNMT1 participates in temperature-responsive development in *Tuta absoluta* [16], and thermal reproductive responses in *Callosobruchus maculatus* involve epigenetic processes [17]. Yet pharmacological inhibition is not mechanism-exclusive, so such experiments cannot identify DNA methylation as a transmitted carrier without additional molecular tracking. In *Acyrthosiphon pisum*, DNMT machinery is expressed in maternal reproductive tissues and perturbation produces developmental and reproductive defects [18]. In *Bemisia tabaci*, Dnmt1-related regulation is associated with oocyte production [19]. These studies establish reproductive or developmental relevance, not transmission of acquired environmental information.

Negative evidence is equally important. Imidacloprid exposure altered bumble-bee gene expression without detectable differential DNA methylation under the tested conditions [20]. Conversely, honey-bee germline

methylation can be maintained with high fidelity while somatic developmental methylation undergoes broader fluctuations that are not necessarily functional [21]. Environmental response, somatic epigenomic change and stable germline methylation are therefore distinct observations. A context-memory interpretation is justified only when the relevant state is shown to persist across the biological transition under discussion.

Histone modification

Histone marks provide clearer examples of both developmental state and mechanistic boundary. In honey-bee larvae, H3K4me1 differs with caste and developmental stage and is associated with caste-specific transcriptional programs [22]. This supports a role in developmental regulation but does not identify H3K4me1 as a germline carrier. Diapause in *Culex pipiens* is likewise tissue specific: H3K27me2 is reduced in fat body but not ovaries [23]. A whole-animal "epigenetic diapause state" would therefore erase a biologically important compartment boundary.

The strongest causal evidence in this section comes from Drosophila reproductive diapause. Ovary-specific manipulation of histone methylation regulators shows that histone methylation can alter diapause propensity within a defined genotype, while descendant phenotypic effects diminish across generations [24]. The experiment therefore supports causal regulation of diapause and multigenerational phenotype persistence, but it does not demonstrate that the altered histone marks themselves are the inherited molecular carrier.

The interpretive question is not which histone mark is "most epigenetic," but what inference each evidence pattern permits. The distinctions are more efficiently resolved as a state-by-evidence decision matrix because tissue restriction, developmental regulation and descendant persistence impose different limits on mechanistic interpretation.

Table 1. Histone-state evidence separates developmental regulation, tissue restriction and inherited-carrier claims in insects

Histone-state distinction	Biological context with observed basis	Permissible interpretation, boundary or uncertainty, and discriminating next test
Caste-associated H3K4me1	Honey-bee larval caste differentiation Stage- and caste-linked histone and transcription profiles	Histone state participates in developmental regulation Association does not establish meiotic persistence Track the same mark through defined developmental transitions and perturb its maintenance
Parent-of-origin histone association	Honey-bee reciprocal-cross caste development Allele-specific transcription with histone-state differences	Parent-of-origin regulation can be histone-associated Parent-of-origin expression is not equivalent to environmental inheritance Separate inherited allele effects from inducible chromatin-state persistence
Tissue-restricted H3K27me2 shift	Mosquito adult diapause Fat-body change with ovarian null	Histone response can be compartment-specific Whole-organism generalization is unsupported Test persistence independently in responsive and nonresponsive tissues
Histone-regulated diapause with descendant phenotype	Drosophila reproductive diapause Tissue-specific perturbation plus descendant phenotyping	Histone methylation can causally regulate diapause; descendant effects can persist Molecular carrier across generations remains unidentified Track candidate histone states in germ cells and unexposed descendants

Noncoding RNA

Noncoding RNAs widen the mechanistic landscape because they can regulate development, interact with other epigenetic systems and occur in the germline, yet none of those properties alone demonstrates inherited environmental memory. Drosophila miRNAs regulate multiple stage- and tissue-specific developmental processes [25]. In honey bees, a transposable-element-derived miRNA provides stronger causal evidence: experimental elevation of the miRNA suppresses DNMT3 and biases development toward queen-like traits in the tested caste-differentiation window [26]. The result demonstrates cross-layer regulation between RNA and methylation machinery, not transgenerational transmission.

The germline adds another level of inference. Drosophila ovarian piRNA clusters form a specialized, evolutionarily dynamic small-RNA system [27]. Their germline localization makes them biologically relevant to

inheritance questions, but localization is only competence, not proof that environmental information has been encoded, retained and transmitted. Developmental miRNA regulation, miRNA–DNMT coupling and germline piRNA architecture therefore represent different mechanistic roles rather than interchangeable evidence for epigenetic inheritance.

A visual boundary map is needed here because the central distinction is relational rather than taxonomic: regulatory action, persistence and access to the germline occupy different evidential positions even when all involve noncoding RNA.

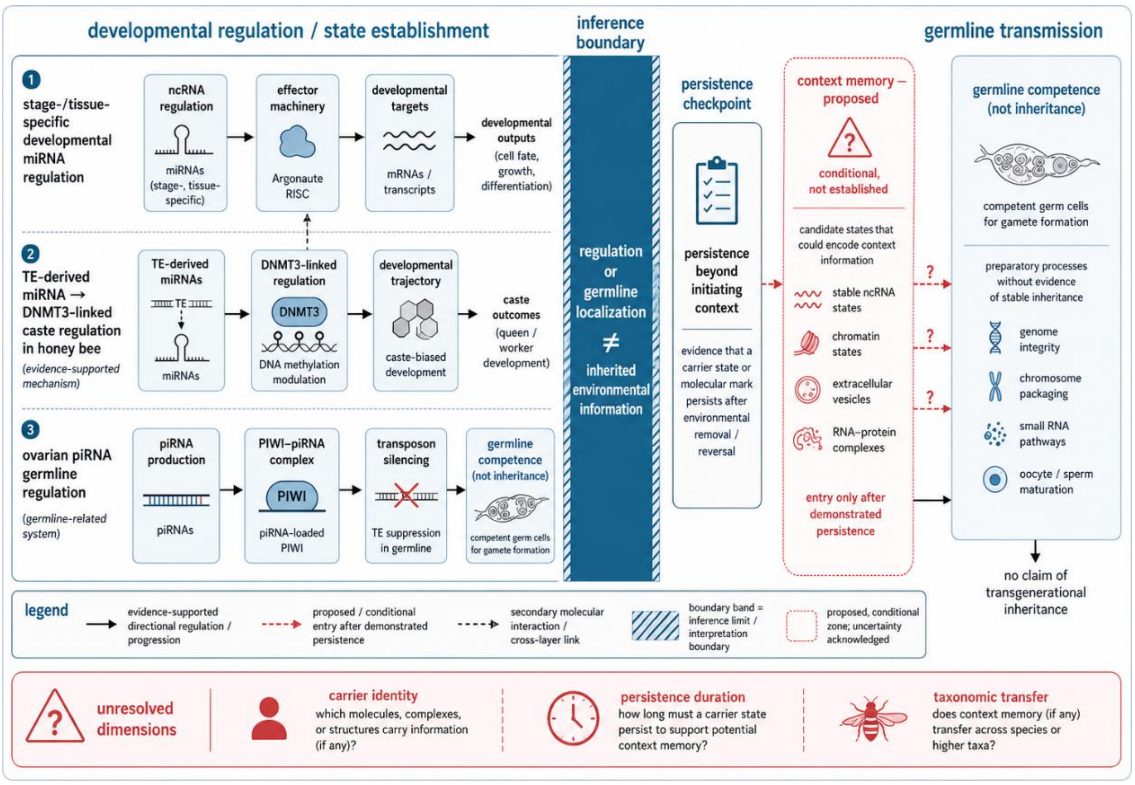


Figure 1. Noncoding-RNA regulation occupies different positions between developmental control and heritable information

Persistence across development

Persistence is the point at which an epigenetic response begins to resemble memory, but the biological level must be specified. Chromatin can be propagated through mitotic divisions by replication-coupled and post-replicative mechanisms, providing a mechanistic basis for cellular memory without requiring meiosis or organismal inheritance [28]. This lower-level principle is relevant to insects as a mechanistic possibility; it does not establish that a particular insect environmental response survives development.

Insect studies instead reveal several persistence patterns. Honey-bee caste-associated chromatin states remain organized across larval differentiation [10]. Related chromatin-state evidence likewise supports persistent developmental divergence between queen and worker trajectories [11]. By contrast, bumble-bee methylation shows evidence consistent with developmental erasure in defined sex and tissue contexts [14], while honey-bee germline methylation can remain comparatively stable even as somatic methylation fluctuates [21]. Persistence is therefore not a property of "the epigenome" as a whole.

The Drosophila diapause study adds a further distinction: a histone-regulated maternal phenotype can be followed by descendant effects even though the molecular carrier remains unresolved [24]. For this perspective, context memory is proposed only when a molecularly associated state is retained beyond the initiating context and can bias, or is positioned to bias, a later developmental or physiological state. Continued exposure, irreversible differentiation and stable constitutive regulation remain alternative explanations that must be excluded experimentally.

A context–mechanism–outcome register is therefore more informative than listing molecular marks alone, because the same epigenetic class can be established, retained, erased or merely correlated with a descendant phenotype at different biological horizons.

Table 2. Persistence horizon determines what an insect epigenetic state can legitimately be said to remember

Observable outcome linked with required next evidence	Context–mechanism combination	Interpretation/consequen within its limit
Immediate regulatory state *Evidence-derived state; classification proposed*		
Altered transcription or trajectory during the initiating context **Re-measure after the initiating signal or stage has ended**	Accessibility or RNA-linked regulation within one developmental window	Regulatory response, not memory by itself Persistence has not been demonstrated
Developmentally retained state *Proposed context-memory category*		
Divergent developmental trajectory remains organized through successive stages **Demonstrate retention after the initiating cue is absent or altered**	Caste-associated chromatin organization across larval differentiation	Candidate developmental context memory Continuing instructive signals or irreversible differentiation can mimic memory
Rewritten or erased state *Evidence-derived boundary; classification proposed*		
Earlier methylation configuration is reduced, replaced or redistributed **Track matched tissues or cell states across transitions**	Stage-, sex- or tissue-specific methylation remodeling	Reset boundary limits the persistence horizon Cell turnover and tissue composition can produce apparent rewriting
Germline-stable baseline *Evidence-derived distinction*		
Germline state remains stable while somatic state changes **Demonstrate an environmentally induced state change followed by transmission**	Comparatively faithful germline methylation with a more dynamic soma	Germline stability is biologically distinct from somatic persistence Stability does not demonstrate environmental acquisition
Descendant phenotype without resolved carrier *Evidence-derived pattern; carrier inference withheld*		
Phenotype persists beyond the directly manipulated maternal state **Couple descendant phenotype to a specific transmitted molecular state**	Histone-regulated maternal diapause followed by weakening descendant effects	Intergenerational or multigenerational phenotypic persistence The inherited molecular carrier is unidentified

The register deliberately stops short of stable transgenerational inheritance. That stronger category requires evidence about germline passage, exposure-generational structure and molecular carriage that is considered in the next section.

Germline transmission

Germline involvement is the principal boundary between developmental persistence and claims of inherited epigenetic information. A molecular state observed in reproductive tissue is not automatically transmitted, and a phenotype observed in descendants is not automatically epigenetic. Exposure of germ cells, maternal provisioning, altered reproductive physiology and inherited genetic differences can all generate cross-generational resemblance without stable transmission of an acquired epigenetic state [4].

Insect methylation studies illustrate why germline competence and transmission must be separated. In the viviparous pea aphid, DNA-methylation machinery is expressed in maternal reproductive tissues and germ cells and contributes to normal reproduction and development [18]. Honey-bee germline methylation, meanwhile, can be maintained with high fidelity relative to more variable somatic methylation [21]. These findings establish that

methylation machinery and stable methylation states can exist in germline biology; neither demonstrates that an environmentally induced methylation configuration has crossed the germline into an unexposed generation.

A substantially stronger evidential endpoint exists in defined Drosophila Polycomb systems. Stable transgenerational inheritance of a chromatin state has been experimentally demonstrated, and subsequent work identifies interchromosomal contacts and PRC2-dependent chromatin regulation as mechanistically important in the same experimental architecture [29, 30]. These studies establish that stable chromatin-based transgenerational inheritance is biologically possible in insects, but they do so in highly defined Drosophila loci. They should therefore function as proof of mechanism rather than evidence that stable epigenetic inheritance commonly follows environmental exposure across insect taxa.

Mechanistic non-equivalence remains important even at this high evidential level. In the Fab2L Polycomb system, disruption of small-RNA pathways did not abolish direct initiation or maintenance of the inherited state, indicating that small RNAs are not obligatory carriers in this particular form of Drosophila transgenerational epigenetic inheritance [31]. The finding does not exclude small-RNA-mediated inheritance elsewhere; instead, it demonstrates that "epigenetic inheritance" cannot legitimately be assigned a universal molecular carrier.

Accordingly, stable transgenerational inheritance should be inferred only after genetic transmission, continued or direct exposure and other parental effects have been separated from the proposed epigenetic mechanism [32]. Germline localization, descendant phenotype, molecular persistence and mechanistic transmission are complementary observations, not interchangeable substitutes.

Context memory versus stable inheritance

The proposed concept of context memory is intended to preserve this evidential separation. Chromatin biology establishes that epigenetic states can persist through mitotic cell divisions [28], but such cell memory neither requires nor demonstrates transmission through meiosis. At the other extreme, stable transgenerational inheritance requires a substantially stronger combination of generational and mechanistic evidence [5]. Context memory occupies the interpretive space between these endpoints.

In this perspective, context memory is proposed to mean an epigenetically associated molecular state that outlasts the developmental or environmental condition that established it sufficiently to alter the probability or direction of a later molecular, physiological or developmental response. Three restrictions are essential. First, persistence must extend beyond the initiating context rather than merely accompany it. Second, the retained state must be linked to a later response rather than inferred from a static molecular difference. Third, the designation does not imply meiotic inheritance, adaptation or fitness benefit.

This formulation distinguishes persistence horizon from carrier resolution. Drosophila reproductive diapause provides an instructive intermediate case: histone methylation can causally influence the maternal diapause phenotype, and descendant effects can persist, yet the molecular entity transmitted between generations remains unresolved [24]. By contrast, experimentally controlled Polycomb inheritance provides much stronger evidence connecting a persistent chromatin state to a defined transgenerational mechanism [30]. These cases should not be combined simply because both extend beyond an initial developmental context.

Negative evidence further constrains the framework. Bumble-bee transcription can respond to an environmental toxicant without detectable DNA-methylation change [20]. Conversely, stable Polycomb inheritance can proceed without direct small-RNA initiation or maintenance in the tested Drosophila system [31]. Context memory therefore cannot be diagnosed by the presence of any single favored epigenetic mark. It is a proposed relationship among state establishment, persistence horizon, later functional bias and level of transmission.

The resulting evidential landscape is best represented as a coverage-and-gap map because the central problem is not ranking mechanisms but identifying which inferential links have actually been demonstrated.

Table 3. Evidence coverage and unresolved transitions between proposed context memory and stable epigenetic inheritance

What can be concluded within its limit	Biological evidence requ and decisive check	Research test needed
	Immediate epigenetic response	
	Evidence class	
Molecular response to the initiating condition	Context-associated change in accessibility, methylation, histone state or ncRNA regulation	Resample after context withdrawal or
Persistence after the condition ends	Calling co-occurrence "memory"	developmental transition

Developmentally persistent state ***Proposed context-memory class***		
Candidate context memory if later response is biased **Independence from continuing developmental instruction**	Same or mechanistically linked state retained across a later developmental interval Confusing differentiation with memory	Remove or alter the initiating context and test retention
Germline competence ***Evidence class***		
Molecular access to the germline **Whether acquired information is transmitted**	Relevant mechanism or state present in germ cells/reproductive tissues Germline presence interpreted as inheritance	Track an induced state through gametes and descendants
Descendant phenotype with unresolved carrier ***Evidence class***		
Intergenerational or multigenerational persistence **Molecular carrier and exclusion of parental alternatives**	Phenotypic effect persists into descendants Phenotype persistence equated with epigenetic TEI	Couple phenotype to a transmitted molecular state
Mechanistically resolved stable inheritance ***High-evidence endpoint***		
Stable epigenetic inheritance in the tested system **Generality across loci, environments and taxa**	Persistent inherited state linked to a defined chromatin or other molecular mechanism across appropriate generations Proof-of-principle generalized to insects broadly	Replicate mechanism across endogenous loci and independent insect systems
Mechanism-negative or null result ***Boundary evidence***		
Candidate mechanism is not universally required **Alternative carrier or regulatory layer**	Response or inheritance persists despite absence of a candidate mechanism Null generalized beyond tested conditions	Orthogonal assays and alternative-mechanism perturbation

These distinctions also require a cross-scale representation because developmental state, germline access and stable inheritance occupy different biological levels rather than successive boxes in a universal pathway.

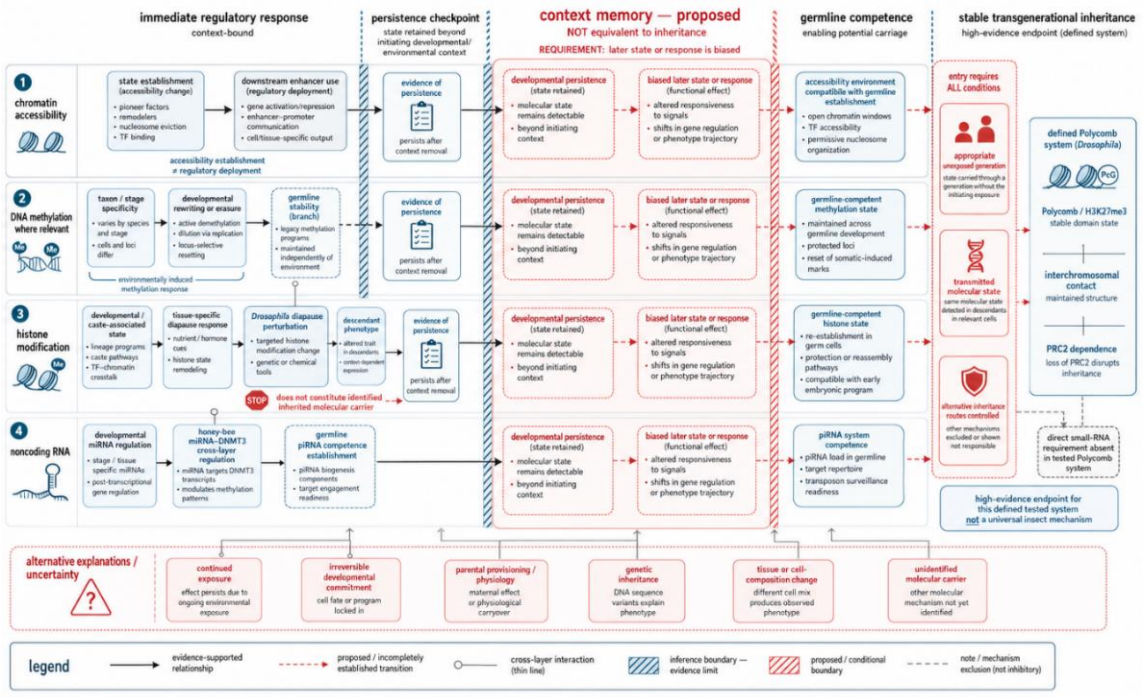


Figure 2. Evidence boundaries separating developmental context memory, germline competence and stable epigenetic inheritance

The central implication of this perspective is that epigenetic regulation in insects is better interpreted as a set of modular, lineage- and context-dependent state processes than as one hereditary program [1]. Comparative methylation evolution alone demonstrates that even a canonical epigenetic mechanism can be extensively reduced, reorganized or absent across insect lineages [13]. Similar caution applies to developmental stage, tissue and sex. The proposed context-memory concept is therefore organizational: it identifies a persistence problem that different molecular mechanisms may solve differently.

Mechanistic confidence should increase only when regulatory perturbation, persistence through the relevant temporal transition and identification of the retained carrier converge. Association studies can identify candidate states, but mechanistic interpretation requires stronger evidence [3]. Drosophila diapause illustrates the value of this distinction because histone perturbation supports within-generation causality while descendant phenotype persistence exceeds current carrier resolution [24]. Rather than weakening such evidence, calibrated terminology makes clear what has and has not been demonstrated.

Environmental and physiological context also restrict transferability. Thermal reproductive responses in a beetle depend on experimental context and are complicated by the specificity of pharmacological epigenetic perturbation [17]. Mosquito diapause provides a different boundary: a histone change detected in fat body is absent from ovaries [23]. These studies make tissue identity, genotype and exposure architecture integral parts of an epigenetic-memory claim rather than nuisance variables.

The proposed framework generates a testable expectation rather than a validated prediction rule: the same environmental driver may produce different persistence horizons according to developmental stage, tissue and molecular layer. Bumble-bee methylation erasure illustrates how a state can be lost at a developmental transition [14], whereas honey-bee miRNA–DNMT3 coupling shows how regulatory information can be redistributed across molecular layers during caste differentiation [26]. Testing context memory therefore requires longitudinal, tissue-aware and mechanism-specific designs rather than single-time-point epigenome comparisons.

Experimental procedures: evidence selection and causal criteria

This article is a structured molecular perspective rather than a systematic review or new experiment. Evidence was selected to resolve specific mechanistic and inferential questions across chromatin accessibility, DNA methylation, histone modification, noncoding RNA, developmental persistence and germline transmission. Direct insect experiments were prioritized for mechanistic claims, whereas critical reviews were used primarily to define evidential boundaries and causal terminology [3].

Causal wording was calibrated to study design. Mechanistically validated perturbation studies were treated differently from correlated omics profiles; for example, experimentally resolved accessibility mechanisms permit stronger directional claims than accessibility differences alone [7]. Association, localization and molecular co-occurrence were not interpreted as causal persistence unless the source design directly supported that inference.

Transgenerational claims required explicit separation of directly exposed generations from later descendants and consideration of germline transmission, genetic inheritance and parental effects [4]. Stable inheritance terminology was reserved for evidence satisfying these stronger conditions rather than for any multigenerational phenotype [32]. No numerical certainty score was assigned because the relevant evidence dimensions are not interchangeable.

Null findings were retained as mechanistic constraints rather than discarded as inconsistency. The absence of detectable methylation change during an exposure-associated transcriptional response limits methylation-specific interpretation under those conditions [20]. Likewise, the absence of a direct small-RNA requirement in a defined Polycomb inheritance system restricts claims of universal RNA-mediated transmission [31]. Across all evidence classes, taxon, developmental stage, tissue, exposure regime and laboratory setting were treated as boundaries on transferability.

Conclusion

Epigenetic regulation can plausibly function as context memory in insects, but only when molecular persistence is demonstrated beyond the context that established the state and linked to a later biological response. This proposed category is intentionally distinct from immediate epigenetic response, germline competence and stable transgenerational inheritance. Chromatin accessibility, DNA methylation, histone modification and noncoding RNA each provide relevant but non-equivalent evidence, with substantial taxonomic, tissue and developmental

constraints. Stable epigenetic inheritance remains a higher evidential endpoint requiring explicit generational and mechanistic support. Treating persistence horizon, carrier identity and biological level as separate questions provides a more defensible basis for connecting insect developmental plasticity with environmental effects across generations.

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