Eurasia Specialized Veterinary Publication

Entomological Research Letters

ISSN: 3108-639X

2021, Volume 1, Issue 2, Page No: 61-70
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Available online at: www.esvpub.com/

Nutrient Sensing and Hormonal State Jointly Regulate Insect Life-History Decisions Beyond Simple Energetic Constraint

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ABSTRACT

Insect life-history responses to nutrition are often described as consequences of energetic or substrate limitation: growth slows when resources decline, reproduction contracts when nutrient supply is inadequate, and survival trade-offs emerge when allocation becomes constrained. This interpretation is necessary but incomplete. Nutrients also act as regulatory information, while juvenile hormone, ecdysteroids, insulin/insulin-like growth factor signaling, target of rapamycin, AMP-activated protein kinase, neuropeptides, and tissue-specific endocrine responses determine how nutritional information is converted into developmental or reproductive action. This article develops a molecular-physiological model in which insect life-history decisions depend on the joint configuration of nutrient identity and availability, endocrine state, developmental or reproductive state, and tissue-specific signal responsiveness. Evidence from *Drosophila*, mosquitoes, *Bombyx*, *Manduca*, and other insects indicates that similar nutritional inputs can yield different outcomes across stages, sexes, genotypes, and taxa, and that hormonal state can itself alter nutrient acquisition, metabolic processing, and pathway sensitivity. The proposed model therefore treats nutrition as a state-dependent signal rather than a scalar energetic input. It generates testable predictions about when identical nutritional environments should produce divergent life-history outputs and identifies the experimental boundaries required to distinguish causal signaling from correlated physiological state.

Keywords: Nutrient sensing, Insulin/TOR signaling, Juvenile hormone, Ecdysteroids, Insect life history, Endocrine crosstalk

Received: 17 October 2021
Revised: 29 November 2021
Accepted: 03 December 2021

How to Cite This Article: Lahtinen M, Salo E, Virtanen J. Nutrient Sensing and Hormonal State Jointly Regulate Insect Life-History Decisions Beyond Simple Energetic Constraint. Entomol Res Lett. 2021;1(2):61-70.
https://doi.org/10.51847/5JIyocAX2i

Introduction

Nutrition is indispensable to insect growth, maturation, reproduction, and survival, but the common language of energetic constraint can obscure how nutritional information is physiologically interpreted. In *Drosophila*, reproductive output depends not only on substrates required for oogenesis but also on nutrient-responsive endocrine and developmental programs; broader insect evidence similarly places juvenile hormone (JH), ecdysteroids, and insulin-related signaling within interacting regulatory networks [1–3]. The central inferential problem is therefore not whether energy matters. It is whether a given amount or composition of food can be expected to produce a particular life-history outcome independently of hormonal and physiological state. The available evidence indicates that it cannot.

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Two observations make a scalar energetic model especially inadequate. First, nutritional effects can carry a temporal signature. In *Drosophila melanogaster*, current and ancestral diets interact in trait-specific ways across development and reproduction, showing that present intake does not fully specify the organismal response [4]. Second, genetic background can strongly alter the lifespan response to dietary restriction; across a large *Drosophila* genotype panel, the same nutritional intervention produced heterogeneous outcomes associated with genetic and metabolomic variation [5]. Neither observation removes energetic limitation from the causal system. Instead, both show that nutritional input is filtered through state variables that change the mapping between intake and phenotype.

This article develops a proposed joint-state model for insect life-history regulation. The model distinguishes four analytical elements that are often collapsed: nutrient input, nutrient-sensing pathway activity, endocrine state, and the downstream life-history decision. It further separates direct molecular mechanism from association, laboratory response from field-level inference, and plastic physiological response from evolutionary adaptation. The central claim is deliberately conditional: nutrient sensing and hormonal state jointly determine the regulatory meaning of nutritional information, but the topology and strength of that coupling need not be conserved across tissues, stages, sexes, or taxa. The following sections build this argument from nutrient-sensing architecture through IIS/TOR/AMPK signaling, JH and ecdysteroid state, and their crosstalk before considering discrete life-history decision nodes.

Nutrient-sensing architecture

A useful nutrient-sensing architecture must specify where information is detected, what property of nutrition is detected, how that information reaches endocrine effectors, and which developmental state receives the signal. In *Drosophila* larvae, the prothoracic gland itself participates in a nutrient-sensitive developmental checkpoint: TOR-dependent endocycling in steroidogenic cells supports ecdysteroidogenic capacity and metamorphic timing, while starvation sensitivity changes around the critical-weight transition [6]. This is not simply a whole-animal energy-store effect. A defined cellular program in an endocrine organ changes whether nutritional deprivation can still delay development.

Nutrient identity also matters. Sugar-responsive enteroendocrine neuropeptide F in the *Drosophila* midgut modifies glucagon-like adipokinetic hormone and insulin-like outputs, linking a particular dietary component to systemic lipid metabolism [7]. Conversely, the physiological meaning of an insulin-like signal is not fixed across ontogeny: DILP1 has different metabolic and life-history effects in pupal and adult states [8]. These findings motivate two separations in the proposed architecture. Nutrient amount must be distinguished from nutrient identity, and endocrine-signal identity must be distinguished from the developmental state in which that signal is received.

The architecture is also bidirectional rather than purely feed-forward. In adult *Drosophila*, protein intake induces the fat-body hormone FIT, which feeds back through insulin-related signaling to suppress further protein feeding [9]. Thus, nutrient detection can modify subsequent nutrient acquisition. At the same time, signals unrelated to food quantity can reshape insulin-like growth regulation. Activation of Toll signaling in the larval fat body suppresses Dilp6 and systemic growth, and restoration of Dilp6 can rescue the growth deficit [10]. Immune state is therefore capable of altering a pathway commonly interpreted as nutritionally regulated.

Taken together, these studies support a layered architecture with at least three separable functions: peripheral nutrient discrimination, endocrine relay or modulation, and state-dependent tissue response. They do not establish a universal insect circuit. Most direct molecular evidence comes from *Drosophila*, and relevant sensors, peptides, and endocrine organs can differ among orders. The proposed model therefore treats “nutrient sensing” as a functional category whose molecular implementation must be specified for each taxon, life stage, and tissue.

Insulin/tor and ampk signaling

IIS and TOR are frequently described as canonical conduits between nutrition and growth or reproduction, but their interpretation depends on what is being sensed and on concurrent endocrine state. Amino-acid composition can shift reproduction and lifespan in *Drosophila* even when a simple calorie-based interpretation would predict similar outcomes, with IIS/TOR and other amino-acid-responsive pathways implicated in those effects [11]. The important point is not that energy content becomes irrelevant, but that composition can change pathway activation and therefore change the physiological value of an energetically similar diet.

AMPK adds another layer because it can connect energetic stress and hormonal state. In *Bombyx* and *Drosophila*, 20-hydroxyecdysone (20E) activates an AMPK–PP2A axis that reduces insulin-receptor and AKT phosphorylation and restricts growth-related output [12]. This relationship reverses the simplest nutritional narrative. Rather than nutrients acting upstream of an otherwise passive endocrine system, steroid state can actively reconfigure insulin signaling. A life-history decision based on IIS activity therefore cannot be interpreted without asking whether the relevant tissue is simultaneously under steroidal control.

The response is also conditional on sex. Defined-diet experiments in adult *Drosophila* show that nutrient requirements associated with lifespan differ between males and females, with female oogenesis contributing to that asymmetry [13]. Reproductive investment is therefore not merely an endpoint of nutrient sensing; it helps define the nutrient requirements against which survival is measured. A model that uses "nutritional state" without sex or reproductive condition risks conflating different physiological problems.

Equally important is negative evidence. Protein deprivation in adult female *Drosophila* lowers egg production and gonadal ecdysone titers, but experimentally reduced ecdysone does not account for the accompanying increase in protein appetite [14]. The hormone change is real, yet it is not the demonstrated mediator of the feeding response. This separates correlation among nutrient state, hormone titer, and behavior from causal pathway identity. Such null mechanistic tests are critical for an integrated model because densely connected endocrine networks make plausible but incorrect mediation stories easy to construct.

Nutritional history can extend beyond the individual's current state. Maternal starvation alters a germline translational program and changes progeny responses to later nutritional stress in *Drosophila* [15]. The finding supports an intergenerational physiological-memory term, but it does not by itself establish adaptive transgenerational inheritance or a field fitness benefit. For the proposed model, IIS/TOR/AMPK signaling is therefore best treated as a conditional regulatory layer whose output depends on nutrient composition, steroidal state, sex, reproductive investment, and physiological history.

Juvenile hormone and ecdysteroid state

JH and ecdysteroids should not be represented as independent dials that separately control reproduction and development. Across insects, JH participates in oogenesis through interactions with tissue-specific, nutritional, and ecdysteroid pathways, but its precise targets and timing differ among reproductive strategies [16]. In adult *Drosophila*, a direct example of endocrine networking is provided by the 20E–ecdysis-triggering hormone (ETH)–JH axis: 20E supports ETH expression, ETH promotes JH production, and disruption of this chain impairs ovarian and egg-production phenotypes [17]. The relevant unit of analysis is therefore an endocrine configuration, not a single circulating hormone concentration.

During juvenile development, JH can also constrain ecdysteroid production directly. Krüppel homolog 1 (Kr-h1), a JH-responsive transcription factor, represses steroidogenic-enzyme transcription in studied *Drosophila* and *Bombyx* systems, while work in the *Drosophila* ring gland demonstrates antagonistic actions of JH and 20E during developmental transitions [18, 19]. These findings justify inhibitory and reciprocal relationships in a state model, but only within the tissues and stages in which they have been demonstrated. They do not imply that every JH–20E interaction is antagonistic.

The same endocrine molecules can participate in qualitatively different decision problems. In *Bombyx*, JH-induced Kr-h1 directly represses E93, preventing precocious larval–adult metamorphosis [20]. Here, endocrine state acts as a transcriptional gate on developmental competence. In adult *Drosophila* follicles, by contrast, local ecdysteroid-receptor signaling contributes to follicle rupture and ovulation [21]. The life-history consequence depends not only on which hormone is present but also on where its receptor-mediated program is active and which developmental transition is available to the tissue.

These examples support a distinction among endocrine restraint, endocrine competence, and endocrine relay. "Restraint" refers to a hormone-dependent state that prevents a transition, as in JH/Kr-h1 repression of metamorphic or steroidogenic programs. "Competence" refers to local tissue responsiveness required for a transition, as in follicular steroid signaling during ovulation. "Relay" refers to hormone-to-hormone coupling, as in the adult 20E–ETH–JH reproductive network. This three-part terminology is proposed here as an analytical classification, not as a claim that all insect endocrine states fall into three immutable categories.

The state configurations developed above are difficult to compare in prose because they differ simultaneously in tissue, life stage, direction of regulation, and inferential status. The following comparison therefore separates the demonstrated endocrine relation from the biological context in which that relation can legitimately be interpreted.

Table 1. Endocrine-state configurations that separate restraint, competence, and relay in JH–ecdysteroid control of insect life-history transitions

Hormonal state		Functional classification	
Endocrine configuration	**Site and stage evidence**	**Regulatory role**	**Experimental boundary**
Reproductive-state signaling			
JH-supported reproductive signaling	Adult female oogenesis across multiple insect systems. JH-dependent ovarian and reproductive processes vary with reproductive strategy and endocrine context	JH is better treated as a reproductive-state signal than an invariant reproductive "on" switch. Evidence-supported pattern.	Targets and interactions differ among taxa and stages. Resolve tissue-specific JH targets under defined nutritional states
20E→ETH→JH endocrine relay	Adult female Drosophila reproduction. Perturbation of the hormone-to-peptide-to-hormone sequence changes ovarian, yolk, and egg-production phenotypes	Reproductive state can be maintained through serial endocrine coupling. Evidence-supported relationship.	Demonstrated in a specific adult Drosophila network. Test for analogous relays without assuming conserved topology
Developmental restraint and competence			
JH/Kr-h1 restraint of steroidogenesis	Larval Drosophila and Bombyx steroidogenic systems. Kr-h1 directly represses steroidogenic-enzyme transcription	JH state can reduce developmental steroidogenic competence through transcriptional control. Evidence-supported relationship.	Direction and targets are tissue- and stage-dependent. Measure JH/Kr-h1 and steroidogenic output in the same tissue and temporal window
Reciprocal JH–20E developmental antagonism	Drosophila ring gland during developmental transition. Manipulating either endocrine arm alters the opposing biosynthetic state and transition timing	Developmental endocrine state can be reciprocal rather than hierarchically one-way. Evidence-supported relationship.	Not established for every tissue or insect. Test reciprocity rather than infer it from opposing hormone titers
JH/Kr-h1 repression of E93	Bombyx larval–adult transition. Direct transcriptional repression of a metamorphic competence factor	Endocrine restraint can preserve the current developmental state by blocking transition competence. Evidence-supported relationship.	Does not itself demonstrate nutritional control. Couple endocrine-gate assays to defined nutrient manipulations
Local follicular steroid competence	Mature Drosophila follicles. Follicle-specific ecdysteroid-receptor signaling is required for normal rupture and ovulation	Local receptor state can determine whether a systemic reproductive program is executable. Evidence-supported relationship.	Local tissue response cannot be inferred from circulating titer alone. Pair systemic hormone measurement with tissue-specific receptor/output assays
Cross-case synthesis			
Restraint–competence–relay classification	Cross-case synthesis of the mechanisms above. Comparison of inhibitory gates, local permissive responses, and serial endocrine coupling	Provides a vocabulary for distinguishing how hormonal state enters a life-history decision. Proposed synthesis.	Classification has not been prospectively validated across taxa. Test whether classes remain separable and whether mixed states occur

The same evidence also requires a visual representation in which endocrine state is a trajectory with alternative locally available transitions rather than a list of isolated pathways. **Figure 1** places nutrient-responsive signaling alongside developmental and reproductive endocrine states while keeping demonstrated connections distinct from proposed cross-state integration.

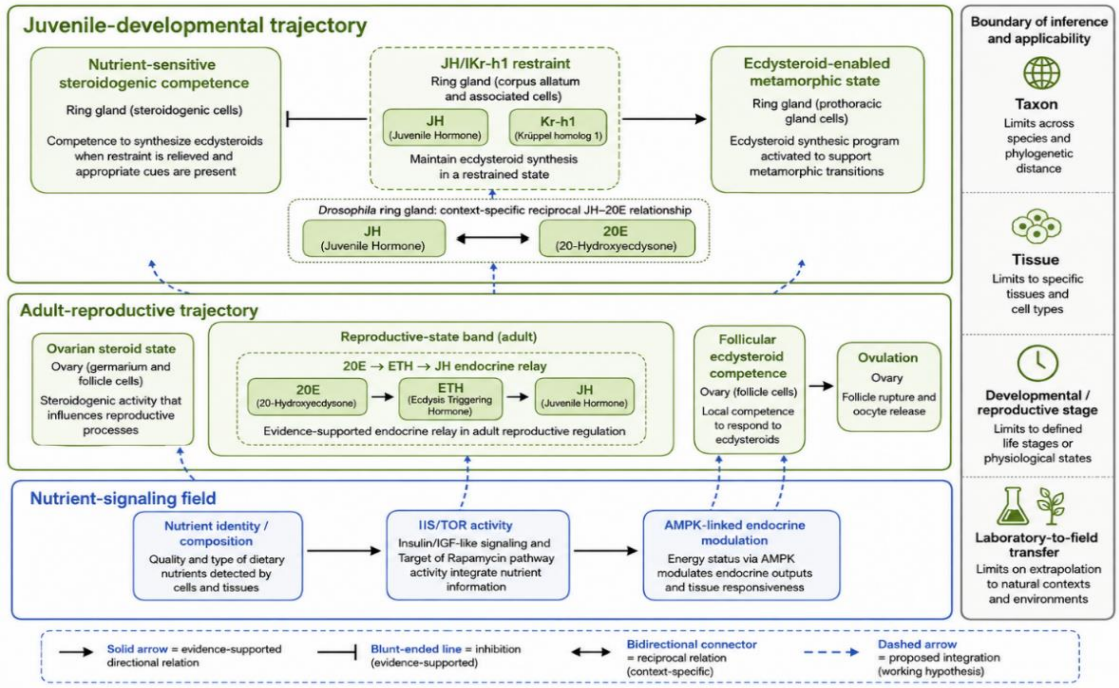


Figure 1. Endocrine trajectories distinguish developmental restraint, steroidogenic competence, and reproductive relay under state-dependent nutrient signaling

Crosstalk between nutrient and endocrine signals

The preceding sections establish that nutrient-responsive pathways and endocrine pathways are individually state dependent. Crosstalk becomes important when one system changes the regulatory meaning of the other. In adult female *Aedes aegypti*, JH- and 20E-responsive transcriptional regulators differentially control insulin-like peptide genes across the gonotrophic cycle [22]. The implication is not a single hormone-to-IIS arrow. Different endocrine phases alter which insulin-like signals are produced and therefore change how metabolic regulation is configured before and after blood feeding.

Comparative developmental evidence provides an equally important constraint. *Manduca sexta* and *Drosophila melanogaster* both undergo nutritional-developmental transitions, but prothoracic-gland activity does not retain the same relationship to nutrition after those transitions, and JH contributes differently to timing in *Manduca* [23]. Similar life-history outcomes can therefore arise from different nutrient–endocrine couplings. This is a direct warning against treating "critical weight" or steroidogenic commitment as a conserved molecular module merely because the organismal phenotype appears analogous.

Crosstalk also operates across biological levels. Nutrient-responsive IIS, TOR, and related signals regulate adult female germline stem cells through local niche and systemic mechanisms in *Drosophila* [24]. At a broader organ scale, ovarian ecdysone after mating promotes gut stem-cell activity and intestinal remodeling; the resulting physiological plasticity supports reproductive output but is accompanied by increased dysplasia or tumor susceptibility [25]. Cellular activation, organ remodeling, and organismal consequence are therefore distinct levels of analysis. A reproductive benefit at one level cannot be translated automatically into lifetime fitness or population advantage.

Finally, not every signal arriving at an endocrine organ is itself a nutrient sensor. Multiple neuropeptides and peptide hormones can regulate ecdysone production in *Drosophila*, transmitting environmental, developmental, or nutritional information directly or indirectly to the prothoracic gland [26]. This distinction matters because a densely connected endocrine system can make upstream association look like direct nutrient sensing.

In the proposed joint-state model, crosstalk is therefore defined operationally as a change in the response of one regulatory layer caused by the state of another. Such crosstalk may be directional, reciprocal, tissue-restricted, or temporally gated. Its interpretation must retain the specific taxon, life stage, tissue, reproductive condition, and experimental setting in which the relationship was demonstrated. The resulting architecture differs fundamentally from a simple energetic-constraint model: nutritional information is not assigned a fixed physiological value before it enters the endocrine system. Its regulatory meaning emerges from the state of the system that receives it.

Life-history decision nodes

Life-history "decision nodes" are used here physiologically: transitions whose execution depends on converging environmental, nutritional, endocrine, and tissue-state information. In *Drosophila*, dormancy-inducing conditions engage clock-neuron peptides and insulin-producing cells, with insulin-like signaling acting against reproductive dormancy in the studied paradigm [27]. This supports endocrine gating of dormancy, not a universal mechanism for insect diapause.

Repeated reproduction creates a different transition. In *Aedes aegypti*, 20E-induced E93 is required for termination and resetting of the gonotrophic program, including HR3- and autophagy-associated shutdown of translation, yolk, and metabolic programs [28]. In *Colaphellus bowringi*, diapause-inducing photoperiod reduces ecdysteroid state, while 20E manipulation shifts vitellogenesis and fat accumulation through JH-linked and JH-independent components [29]. These systems therefore differ in environmental trigger, endocrine direction, temporal organization, and endpoint.

Reproductive state can also feed back to nutrient acquisition. In mated female *Drosophila*, endocrine and enteroendocrine signals remodel enteric neural and crop physiology to increase feeding; disrupting this response reduces reproductive output [30]. Conversely, thermal or nutritional stress can elevate ecdysteroid state while reducing ETH-dependent reproductive support, suppressing oogenesis and ovulation; ETH supplementation mitigates parts of this response [31]. Such arrest should not be reduced to immediate energetic shortage or presumed adaptive without fitness evidence.

Across these cases, entry, reset, feedback, diapause preparation, and arrest are non-equivalent regulatory operations. **Table 2** compares them by decision logic rather than by presumed energetic severity.

Table 2. Distinguishing insect life-history decision nodes by transition logic, endocrine state, and evidential boundary

Transition node			Validation boundary	
Life-history transition	**Taxon/state evidence**	**Decision logic**	**What cannot be generalized**	**Falsification and standing**
Dormancy entry	Adult female Drosophila. Clock-peptide/IIS interaction under dormancy induction	Neuroendocrine gating of reproductive-state entry	Not equivalent to all insect diapause	Manipulate induction conditions and IIS jointly. Evidence-supported.
Gonotrophic reset	Adult female Aedes aegypti. 20E-induced E93 terminates/resets the preceding program	One reproductive state must be terminated before the next	Blood-feeding cycle specific	Separate cycle termination from initiation. Evidence-supported.
Photoperiodic diapause preparation	Adult female C. bowringi. Photoperiod alters ecdysteroid state; 20E changes vitellogenesis/fat accumulation	Environmental timing redirects endocrine/allocation state	Steroid direction not universal across diapause systems	Factorially test photoperiod and hormone state. Evidence-supported.
Reproductive-demand feedback	Mated female Drosophila. Reproductive state increases enteric feeding drive	Life-history state modifies subsequent nutrient acquisition	Increased feeding ≠ lifetime fitness benefit	Measure feedback as well as nutrient effects on reproduction. Evidence-supported.
Stress-induced arrest	Adult female Drosophila. Stress alters 20E–ETH–JH/octopaminergic support	Competing physiological state interrupts reproduction	Acute laboratory stress ≠ adaptive benefit	Distinguish endocrine mediation from generalized deficit. Evidence-supported.
Transition/reset/feedback/arrest classes	Cross-case comparison. Synthesis of the operations above	Separates how joint state changes life-history execution	Classes may overlap across taxa	Test under factorial nutrient × endocrine manipulations. Proposed synthesis.

Because these nodes occupy different temporal regimes and biological levels, **Figure 2** reconciles them without forcing taxon-specific pathways into one conserved mechanism.

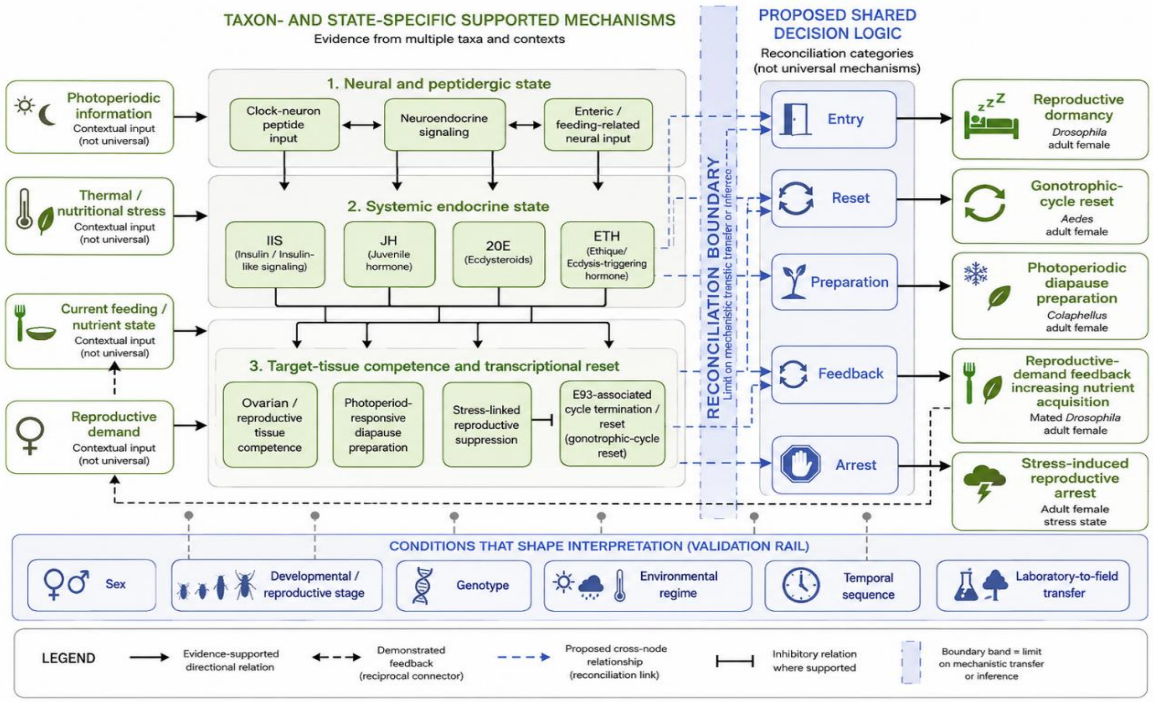


Figure 2. Life-history outputs diverge when nutritional information meets different endocrine and temporal states

Integrated regulatory model and testable predictions

The proposed joint-state model treats life-history output as conditional on nutrient identity and availability, endocrine configuration, tissue or developmental competence, and contextual history. It is conceptual rather than fitted and assigns no universal weights or thresholds.

Its first prediction is state dependence. Nutrient-sensitive prothoracic-gland control shows that developmental state changes the consequence of nutritional deprivation [6], while 20E–AMPK–PP2A signaling shows that steroid state can reconfigure IIS [12]. In adult *Aedes*, endocrine phase also changes ILP regulation [22]. Thus, identical nutritional inputs should not be expected to produce identical outcomes when endocrine or tissue state differs.

Its second prediction is mechanistic non-equivalence. *Manduca* and *Drosophila* can reach superficially similar developmental transitions through different nutrient–endocrine dependencies [23]. Similar outcomes therefore need not imply conserved pathway topology.

Third, reproductive dormancy, photoperiodic diapause preparation, and stress-induced reproductive arrest all suppress reproduction but arise through distinct regulatory configurations [27, 29, 31]. The model predicts that classifying them only by reduced reproductive output will obscure meaningful mechanism.

The model also predicts directional asymmetry. Nutritional state may alter endocrine output, yet endocrine state can simultaneously alter feeding, tissue sensitivity, or nutrient-processing capacity. Evidence for a nutrient effect at one time point therefore does not establish that nutrition remains the dominant upstream variable throughout a transition. Experiments should resolve sequence: nutrient exposure, pathway activation, endocrine change, tissue response, and life-history execution should be measured at appropriate time scales rather than collapsed into one endpoint.

A fourth prediction concerns local competence. Systemic hormone abundance should be an unreliable proxy when the decisive event depends on receptor state or tissue-specific transcriptional competence. Similar circulating endocrine environments may therefore yield different outcomes because target tissues occupy different developmental or reproductive states. This matters particularly across stages and species, where homologous pathway names can conceal different regulatory roles.

Falsification is possible. If changing endocrine state repeatedly fails to modify a nutritional effect when nutrient intake and tissue state are controlled, then the proposed joint-state interaction is unsupported for that decision. If apparently distinct transitions instead share the same regulatory dependence across broad taxa and contexts, the model's emphasis on mechanistic plurality would require revision.

Validation requires more than correlated hormone titers. Protein deprivation lowers gonadal ecdysone without making low ecdysone the cause of protein appetite [14]. Testing the model therefore requires factorial nutrient × endocrine manipulations, measurement of intervening signaling events, and replication across taxa, stages, sexes, and realistic environments before claims of broad predictive performance.

Physiological boundary conditions

The architecture is broader than any single model-insect pathway but is not universal. Comparative synthesis shows that nutrition alters insect body size through growth-rate and growth-duration mechanisms involving IIS/TOR and developmental hormones, while organ- and taxon-level implementations remain diverse [32].

Sex, reproductive condition, genotype, species, and history all constrain transfer. Male and female *Drosophila* differ in nutritional requirements associated with lifespan [13], while *Manduca* and *Drosophila* differ in post-threshold prothoracic-gland regulation [23]. Dietary responses also vary among genotypes [5], and ancestral or maternal nutritional conditions can modify later phenotypes [4]. Maternal-starvation effects on progeny physiology [15] should not be equated with adaptation, just as nutrient-linked hormone changes should not be promoted to causal mediators when manipulation does not support that inference [14].

Three inference boundaries are especially important. First, molecular response is not synonymous with organismal benefit: altered signaling, growth, feeding, or fecundity does not establish greater lifetime fitness. Second, plasticity is not evidence of adaptation unless evolutionary and fitness consequences are independently demonstrated. Third, mechanistic findings from one tissue cannot be promoted automatically to organism-wide control; local steroid responsiveness may determine whether a transition is executable without making circulating hormone concentration sufficient to predict it.

Environmental transfer also requires caution. Natural food varies in composition, temporal availability, microbial context, and accessibility, while temperature, photoperiod, infection, mating status, and population genotype can alter the same endocrine pathways. Laboratory experiments are strongest for identifying possible regulatory relations and weakest when used alone to estimate how often those relations determine outcomes in heterogeneous field environments.

Most direct mechanisms summarized here derive from controlled laboratory diets, genetic perturbations, or induced endocrine states. The proposed model should therefore function as an architecture for conditional testing, not as a universal insect decision algorithm or a substitute for field validation.

Conclusion

Insect nutrition is both material input and regulatory information. Its life-history meaning depends on endocrine configuration, tissue competence, developmental or reproductive state, and physiological history. The proposed joint-state model replaces a one-directional nutrient-to-phenotype narrative with conditional regulatory logic while preserving taxonomic and experimental boundaries. Its value lies in generating discriminating tests, not in asserting universal pathway conservation or validated predictive performance.

The decisive empirical challenge is comparative and factorial: determine when nutrition changes life history because resources are limiting, when nutrient-sensitive signaling changes endocrine state, and when an apparently identical nutrient signal is interpreted differently because the organism occupies a different physiological state.

Acknowledgments: None

Conflict of Interest: None

Financial Support: None

Ethics Statement: None

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