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Cellular Damage, Repair, Metabolism, and Life-History Reallocation Form an Integrated Regulatory Stressome in Insects

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ABSTRACT

Insects respond to environmental stress through processes usually studied separately: damage formation and recognition, molecular repair, metabolic adjustment, endocrine coordination, and shifts in reproduction or survival-related allocation. Treating them independently can obscure the temporal structure determining whether function is restored, residual injury is tolerated, or impairment persists. This article develops a proposed regulatory stressome model that organizes these processes as interacting but non-equivalent states. It distinguishes exposure from damage, damage-associated signaling from successful repair, molecular protection from organismal performance, and short-term compensation from durable life-history consequences. Evidence from thermal, nutritional, oxidative, cold, and combined-stressor studies shows strong dependence on species, sex, life stage, tissue, exposure history, and environment. Autophagy, DNA repair, mitochondrial remodeling, lysosomal lipid processing, integrated stress signaling, and endocrine pathways provide mechanistic precedents for cross-level coordination, but no evidence establishes a single conserved insect-wide stress network. The proposed stressome therefore treats biological state as a dynamic balance among injury burden, repair capacity, metabolic configuration, endocrine integration, and allocation demands. Recovery and chronic dysregulation are consequently distinguished by trajectories across multiple levels rather than any single stress marker. The framework is a falsifiable organizational model, not a claim of universal mechanism.

Keywords: Insect stress physiology, Cellular repair, Metabolic reprogramming, Endocrine signaling, Life-history allocation, Physiological recovery.

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Introduction

Environmental stress in insects is often described through isolated molecular markers, tolerance limits, or endpoint-specific outcomes, yet these measurements capture different parts of the biological response. Heat tolerance emerges from injury, protective responses, repair, and recovery operating across molecular, cellular, organismal, and ecological scales rather than from a single pathway [1]. The same exposure can therefore produce transient molecular activation, persistent damage, altered reproduction, or little measurable impairment depending on intensity, duration, and biological state.

Stress responses also need not scale monotonically with exposure. Low-intensity challenges can induce stimulatory or hormetic responses involving heat-shock, antioxidant, detoxification, or other defense systems, but

such patterns are conditional and cannot be equated with adaptation or net fitness benefit [2]. Even within one stressor class, responses vary by species and sex. Comparative thermal experiments in *Drosophila melanogaster* and *D. pseudoobscura* show that thermal sensitivity and reproductive responses are not interchangeable across taxa or sexes [3].

The inferential problem addressed here is how damage, repair, metabolic state, endocrine coordination, and life-history allocation can be integrated without collapsing biological levels or overstating causation. This article proposes the insect regulatory stressome as an organizational model linking these components through state-dependent interactions and temporal feedback. Taxon, sex, life stage, tissue, stress history, resource state, and environment are treated as modifiers rather than nuisance variation. The following sections define this stressome and establish the evidence boundaries required before its components can be integrated.

Defining the insect stressome

The stressome is used here in a restricted sense. It is neither a complete inventory of stress-responsive genes and proteins nor a claim that insects possess one conserved master network. The proposed regulatory stressome is the interacting set of damage states, repair capacities, metabolic configurations, endocrine signals, and allocation responses that jointly shape the trajectory from perturbation to recovery or persistent dysfunction.

A first requirement is separating damage from the signals elicited by damage. Heat can increase reactive oxygen species and activate antioxidant responses, yet antioxidant induction does not itself show that oxidative injury was prevented [4]. Chilling can likewise activate immune-related responses through damage-associated molecular patterns and ROS-linked processes in chill-susceptible insects, but such activation cannot automatically be interpreted as beneficial repair [5]. A measured response may indicate attempted compensation, secondary signaling, or incomplete protection. The stressome therefore distinguishes evidence that damaging conditions occurred, evidence that a response pathway was activated, and evidence that function was preserved or restored. Time is equally important. Models incorporating thermal damage, recovery, and repair show that consequences depend not only on exposure but on how injury accumulates and how rapidly function is restored afterward [6]. Two individuals with similar acute markers may thus have different physiological states if their recovery trajectories diverge. Recovery capacity is therefore treated as a core state variable rather than an endpoint appended to exposure.

The model also avoids assuming that regulation is necessarily host-autonomous. In pea aphids, complementary bacterial endosymbionts can together provide a complete mismatch-repair system that restores host heat tolerance, showing that repair competence may sometimes be distributed across a symbiotic unit [7]. This is a specific host-symbiont mechanism, not a general insect rule, but it establishes that relevant stress physiology can extend beyond host tissues when evidence supports such coupling.

Damage detection

“Damage detection” can imply discrete sensors that identify injury and trigger a unified program. The evidence supports a more cautious formulation. Oxidative markers, altered redox state, damage-associated immune signaling, and downstream stress pathways show that cells and tissues respond to disrupted homeostasis, but they do not necessarily identify a single initiating sensor. Here, damage detection means damage-associated signaling sufficient to alter downstream regulatory state, not a universally defined molecular detector.

Reactive oxygen species illustrate the distinction. Under heat, ROS may arise from metabolic disruption and contribute to oxidative injury while antioxidant systems are induced in parallel [4]. A high antioxidant response could therefore reflect effective compensation, severe oxidative challenge, or both. Cold-associated immune activation creates an analogous problem: immune activation after chilling may be triggered by injury signals, while its contribution to protection, repair, or secondary cost remains context dependent [5]. Experimental inference should therefore pair defense markers with non-equivalent measures of injury whenever possible.

The pea aphid symbiosis provides a contrasting case in which a repair-relevant mechanism is more directly resolved. Complementary endosymbiont functions reconstruct a DNA mismatch-repair capability that improves host heat tolerance [7]. Detection, signaling, repair, and tolerance therefore need not occur at the same biological level. In the proposed stressome, these functions may be distributed among intracellular systems, tissues, or interacting organisms.

Cellular repair

Repair helps determine whether detected injury remains transient or becomes a persistent constraint. In *D. melanogaster*, autophagy contributes to heat-stress proteostasis through the handling of damaged or aggregated proteins, linking cellular quality control with thermal tolerance [8]. This supports autophagy as one repair-relevant process but not as a universal determinant of heat resistance; its contribution is expected to depend on tissue, stress severity, and lesion type.

Repair also intersects with metabolism. In *Bombyx mori*, lysosomal acid lipase-1 participates in autophagy and lipid homeostasis through a heat-shock-protein-dependent mechanism [9]. This species-specific result shows that degradation and repair systems can directly interact with substrate handling, creating a plausible route by which cellular maintenance could alter resources available to other functions. Cross-level life-history consequences, however, cannot be inferred from this molecular mechanism alone.

Recovery of organismal function provides another level of evidence. In *Monochamus alternatus*, fertility impaired by heat can recover over time, with heat-shock protein 20 interacting with reproduction-related proteins during recovery [10]. The evidence supports delayed reproductive restoration but not HSP20 as a sufficient causal switch. The proposed stressome therefore represents repair as a trajectory in which molecular responses, tissue function, and reproductive output may recover at different rates.

Metabolic reprogramming

Stress changes both ATP demand and substrate allocation among maintenance, defense, growth, and reproduction. Mitochondria consequently occupy a central but context-dependent position. Under fluctuating thermal regimes, *D. melanogaster* shows coordinated changes in gene expression, mitochondrial physiology, thermal tolerance, and longevity, with some early molecular responses later normalizing [11]. Stress physiology can therefore move through reversible states rather than remaining fixed after initial exposure.

Cold physiology reinforces this contextual interpretation. Different insect cold-survival strategies involve distinct mitochondrial responses in respiration, coupling, metabolic depression, and maintenance of organelle integrity [12]. There is thus no single mitochondrial signature that can serve as the metabolic component of the stressome. The relevant state is the relationship among energetic demand, mitochondrial capacity, substrate availability, and exposure strategy.

Stress history can also persist across developmental transitions. Larval heat exposure in *D. melanogaster* alters adult metabolism and behavior, including metabolic and insulin-signaling-related features [13]. Such carry-over should not automatically be interpreted as adaptive programming; it may represent persistent damage, compensatory remodeling, developmental constraint, or mixtures of these processes.

Specific substrates can connect metabolism with life-history output. In *Loxostege sticticalis*, heat-associated trehalose metabolism accompanies trade-offs between reproduction and survival [14]. This supports substrate handling as a potential mediator of allocation, not a universal resource switch. Likewise, temporally controlled mitochondrial complex-I disruption in *D. melanogaster* has different consequences when imposed during development versus adulthood [15]. Timing therefore changes the meaning of mitochondrial stress.

Within the proposed stressome, metabolic reprogramming means a change in energy production, substrate handling, or metabolic signaling that alters the capacity to sustain repair and other functions. It is intentionally broader than any metabolomic signature. The key inference is whether metabolic change alters the feasible balance among maintenance, recovery, and allocation.

Endocrine coordination

Metabolic state becomes organismally consequential when information about nutrient availability, cellular stress, and tissue condition is communicated across organs. In adult female *D. melanogaster*, the integrated stress response in fat tissue acts as a metabolic sensor during amino-acid deprivation and helps regulate oocyte maturation and ovulation [16]. Refeeding alters this state, illustrating reversible communication between peripheral metabolic condition and reproductive function, but not an insect-wide master stress pathway.

Developmental endocrinology provides a broader precedent. Interorgan signals link tissue growth, nutrient state, and metamorphic timing, showing that endocrine systems can integrate information generated in different organs before major developmental transitions [17]. Ecdysteroid production and secretion likewise integrate multiple developmental inputs through the prothoracic gland and associated signaling pathways [18]. These systems establish distributed endocrine coordination but do not show that adult cellular damage is encoded by identical circuitry.

Reproductive endocrinology adds a taxonomic boundary. Juvenile hormone, ecdysteroids, insulin-like signaling, and related pathways interact in female reproduction, yet their relative functions differ among insect groups [19]. Endocrine coordination is therefore treated here as a functional layer: the mechanisms by which internal-state information alters developmental, reproductive, or maintenance decisions, while the actual hormones, tissues, and pathway hierarchies remain taxon- and stage-dependent.

The distinction also separates coordinated temporary reallocation from a stronger claim of dysregulation. Reversible endocrine adjustment during resource limitation may be compatible with functional coordination, whereas persistent signaling accompanied by unresolved damage would require longitudinal evidence before being classified as chronic failure. **Table 1** therefore distinguishes what endocrine observations can support directly from stressome-level interpretations that remain proposed.

Table 1. Endocrine coordination states that separate demonstrated interorgan regulation from proposed stressome-level inference

Endocrine state and context	Observation and interpretation	Boundary, test, and evidential state
Demonstrated coordination		
Endocrine state or evidence pattern	Observable basis	Boundary condition
Peripheral nutrient-stress sensing coupled to reproduction	Fat-body stress signaling with reproductive response	Restricted by sex, species, nutrient context, and pathway
Biological context	Interpretation	Research implication
Adult female dipteran under amino-acid limitation/refeeding	Reversible metabolic–reproductive coordination	Test comparable coupling across tissues, sexes, taxa, and stressors
		Status
		Evidence-supported mechanism
Endocrine state or evidence pattern	Observable basis	Boundary condition
Interorgan control of developmental timing	Tissue-growth and nutritional signals converging on endocrine timing	Developmental circuitry cannot be transferred directly to adults
Biological context	Interpretation	Research implication
Developing larvae approaching metamorphic transition	Distributed physiological information can regulate developmental commitment	Identify which stress-related inputs enter established developmental endocrine networks
		Status
		Evidence-supported principle
Endocrine state or evidence pattern	Observable basis	Boundary condition
Ecdysteroid integration of developmental inputs	Multiple upstream signals regulating hormone production/secretion	Does not establish ecdysteroids as universal damage sensors
Biological context	Interpretation	Research implication
Insect developmental transition	Endocrine output integrates organismal state	Experimentally separate endocrine integration from damage detection
		Status
		Evidence-supported mechanism
Endocrine state or evidence pattern	Observable basis	Boundary condition
Taxon-dependent reproductive endocrine architecture	Variable roles of juvenile hormone, ecdysteroids, insulin-like and related signals	Strong lineage-, stage-, and tissue-dependence
Biological context	Interpretation	Research implication
Adult female reproduction across insect lineages	Similar reproductive outcomes may use different pathway configurations	Preserve lineage-specific architecture in comparative tests
		Status
		Evidence-supported boundary
Proposed stressome classifications		
Endocrine state or evidence pattern	Observable basis	Boundary condition
Temporary reproductive suppression with later restoration	Reversible endocrine/metabolic signaling and functional recovery	Requires longitudinal molecular and reproductive measurements
Biological context	Interpretation	Research implication
Resource-limited or stressed reproductive state	Compatible with coordinated reallocation	Compare recovery rates across biological levels
		Status
		Proposed stressome classification

Endocrine state or evidence pattern	Observable basis	Boundary condition
Persistent signaling with unresolved damage or reproductive impairment	Continued signaling plus incomplete physiological recovery	No universal diagnostic signature or threshold exists
Biological context	Interpretation	Research implication
Repeated or prolonged stress context	Candidate dysregulation rather than adaptive reallocation	Test whether multi-level persistence predicts failure better than single markers
		Status
		Proposed stressome classification

Life-history reallocation

Stress responses become life-history problems when finite energetic and physiological capacity must be distributed among maintenance, repair, growth, reproduction, and survival. This allocation is not a fixed hierarchy. In *Drosophila melanogaster*, nutritional optima for life-history traits shift with temperature and differ between populations, indicating that resource requirements depend on environmental and population context rather than a universal optimum [20]. Such variation is consistent with the stressome model only if allocation is treated as conditional: an energetic state that supports reproduction under one thermal regime may be inadequate under another.

Sex further alters this landscape. In *Pieris napi*, reproductive traits show sex-specific thermal sensitivity, so similar developmental temperatures do not generate equivalent reproductive consequences in males and females [21]. Survival is also an incomplete proxy for reproductive integrity. Short experimental heatwaves in male *Tribolium castaneum* reduce reproductive performance at temperatures below those causing substantial mortality, demonstrating that a physiologically surviving individual may nevertheless occupy a compromised reproductive state [22]. The stressome therefore separates organismal viability from maintenance of reproductive function.

Longer-term allocation histories add another dimension. Experimental selection for early reproduction in *D. melanogaster* is accompanied by accelerated ageing and extensive metabolic remodeling [23]. This association does not identify a universal metabolite that causes the reproduction–longevity trade-off, but it shows that sustained differences in life-history schedule can coexist with broad changes in metabolic state. Earlier environmental experience can likewise persist across metamorphosis: larval predator exposure produces species- and sex-dependent adult physiological and life-history effects in *Anopheles* mosquitoes [24]. These carry-over effects demonstrate that developmental history can constrain later allocation without establishing whether the resulting phenotype is adaptive, pathological, or simply residual.

Life-history reallocation is therefore defined here as a change in the relative physiological support given to competing functions after stress or altered resource state. It is not inferred merely because reproduction declines. Direct cellular injury, developmental constraint, endocrine suppression, altered substrate availability, or behavioral change can produce similar endpoints. The proposed stressome treats allocation as an integrative output whose interpretation requires evidence about upstream damage, repair, metabolic state, and endocrine context.

Because these relationships span levels and cannot be represented adequately as a single causal chain, **Figure 1** reconciles the evidence-supported components with the article’s proposed cross-level allocation logic while keeping taxonomic, temporal, and inferential boundaries visible.

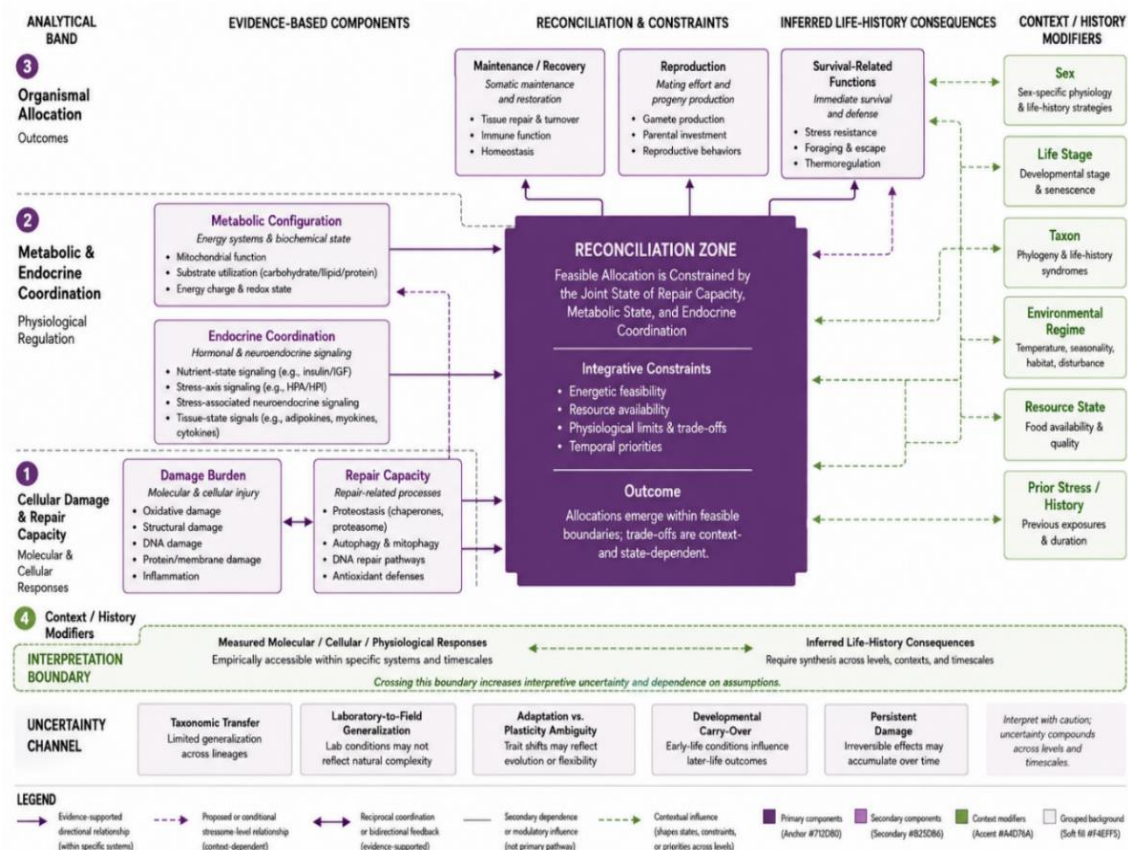


Figure 1. Life-history allocation as a cross-level reconciliation problem within the insect stressome

Recovery versus chronic dysregulation

Recovery is not the simple disappearance of a stress marker. Damage, molecular responses, tissue function, and reproductive performance can normalize on different timescales. Thermal damage–repair models show that post-exposure recovery changes the biological consequence of an otherwise similar stress event [6]. In *Monochamus alternatus*, reproductive function can recover after heat injury [10], whereas fluctuating thermal regimes in *D. melanogaster* produce molecular and mitochondrial responses whose trajectories change through time [11]. These observations argue for a multivariate definition of recovery.

Timing can also alter whether perturbation remains reversible. Developmental and adult mitochondrial complex-I disruption in *Drosophila* produces different organismal outcomes [15], emphasizing that identical categories of molecular perturbation need not have identical consequences across life stages. Similarly, sex-specific reproductive thermal sensitivity means recovery cannot be inferred from one sex or one endpoint [21].

The counterstate, chronic dysregulation, requires greater caution. Combined warming, starvation, and imidacloprid exposure in honey-bee workers does not generate a simple monotonic increase in HSP70 or total antioxidant capacity, while oxidative lipid damage can remain detectable [25]. This demonstrates marker–damage discordance, not a validated syndrome of chronic dysregulation. Accordingly, chronic dysregulation is proposed here as a state in which damage or functional impairment persists while repair, metabolic, endocrine, or allocation responses fail to restore coordinated function across relevant timescales.

The practical distinction is therefore trajectory based. A transient response followed by restoration across molecular and functional endpoints is compatible with recovery. Persistent signaling alone is insufficient evidence of failure, because signaling may remain compensatory. Conversely, normalization of a canonical marker does not prove recovery if damage or reproductive impairment persists. **Table 2** separates these non-equivalent patterns without imposing unsupported thresholds.

Table 2. Trajectories that distinguish coordinated recovery from candidate chronic dysregulation in the proposed insect stressome

Trajectory and context	Observed time-course	Interpretive consequence	Boundary	Longitudinal test and status
Coordinated or compensatory recovery				
Recovery/dysregulation pattern Molecular response resolves and function is restored Biological context Post-stress organism or tissue	Declining stress-response signal together with restored physiological or reproductive function	Compatible with coordinated recovery	Recovery rate may differ among tissues and traits	Test implication Measure repeated molecular and functional endpoints Status Evidence-compatible state
Recovery/dysregulation pattern Molecular response persists while function improves Biological context Ongoing compensatory phase	Continued defense or repair signaling with recovering performance	Persistent signaling need not indicate pathology	Signal may reflect active compensation	Test implication Manipulate pathway while tracking functional recovery Status Proposed stressome classification
Discordant markers and functions				
Recovery/dysregulation pattern Molecular marker normalizes while damage persists Biological context Multiple-stressor or post-stress condition	Weak or normalized canonical marker with continuing oxidative or structural damage	Marker normalization is insufficient evidence of recovery	Damage assay and marker may report different processes	Test implication Pair damage measures with pathway markers longitudinally Status Evidence-supported inference boundary
Recovery/dysregulation pattern Reproductive function remains impaired below lethal limits Biological context Adult or post-developmental thermal stress	Survival maintained but fertility or reproductive traits remain reduced	Organismal survival cannot substitute for recovery of reproduction	Sex, species, and exposure severity alter outcome	Test implication Follow survival and reproduction independently Status Evidence-supported inference boundary
Recovery/dysregulation pattern Developmental perturbation alters later adult state Biological context Stress before metamorphosis or during development	Adult metabolic, behavioral, or physiological differences after earlier exposure	Later phenotype may reflect carry-over rather than ongoing stress	Cannot distinguish damage, compensation, or developmental constraint from endpoint alone	Test implication Use stage-resolved repeated measurements and recovery manipulations Status Evidence-supported boundary
Candidate chronic dysregulation				
Recovery/dysregulation pattern Persistent damage plus unresolved functional impairment across levels Biological context Repeated or prolonged stress	Damage remains while repair, metabolic, or endocrine responses fail to restore function	Candidate chronic dysregulation	No universal duration, threshold, or biomarker is established	Test implication Define system-specific longitudinal failure criteria Status Proposed stressome classification

Integrated regulatory stressome

The proposed regulatory stressome brings these observations together without converting them into a single linear cascade. Its central claim is organizational: damage burden, repair capacity, metabolic configuration, endocrine coordination, and life-history allocation are distinct state variables whose interactions determine the trajectory of stressed insects. The model therefore rejects the assumption that induction of a protective pathway necessarily predicts organismal recovery.

Evidence for each component exists independently. Thermal physiology demonstrates multilevel injury and recovery [1]. Lysosomal lipid processing shows that cellular maintenance can intersect metabolic homeostasis [9]. Trehalose metabolism can accompany reproduction–survival trade-offs under heat [14]. Fat-body integrated stress signaling can coordinate nutrient state with reproduction [16]. The proposed synthesis is that these processes should be studied as coupled constraints rather than as interchangeable markers of a unitary response.

Context is structurally embedded in the model. Species and sex differences in *Drosophila* thermal responses [3], population- and temperature-dependent nutritional optima [20], and developmental carry-over after predator exposure in mosquitoes [24] all show why context cannot be added only after a core mechanism has been specified. In the proposed stressome, taxon, sex, stage, environment, and stress history modify both the available regulatory routes and the meaning of measured endpoints.

This architecture is therefore a reconciliation model rather than a demonstrated molecular pathway. It permits multiple entry points, partial recovery, feedback between energetic state and allocation, and divergence among tissues. It also permits failure without requiring every component to fail simultaneously. Its value depends on whether these distinctions generate predictions that outperform single-marker interpretations.

Testable network predictions

The first prediction is temporal uncoupling. If repair, metabolic adjustment, and organismal performance are distinct state variables, their peaks and recovery rates should not consistently coincide. Fertility recovery after heat [10], changing molecular and mitochondrial responses under fluctuating temperature [11], and stage-dependent consequences of mitochondrial perturbation [15] provide precedents. A direct test would repeatedly measure damage, repair activity, metabolic function, endocrine state, and performance in the same individuals or matched cohorts during exposure and recovery.

The second prediction concerns context-sensitive topology. If the stressome is not universal, the strongest functional connections should differ among species, sexes, stages, and environmental histories. Comparative thermal evidence already reveals species and sex heterogeneity [3], while combined stress in honey bees shows that canonical markers can decouple from oxidative damage [25]. Cross-taxon experiments should therefore test whether shared phenotypic outcomes arise through different regulatory routes rather than assuming conserved pathway weights.

The third prediction is that life-history impairment will sometimes emerge before survival failure. Sublethal reproductive damage [22] makes this directly plausible. The model predicts that reproductive, developmental, or maintenance endpoints may identify loss of coordinated function earlier than mortality-based assays. This is a falsifiable prediction, not a validated forecasting tool.

Finally, recovery should be better characterized by convergence among several biological levels than by normalization of one biomarker. Failure of this prediction—if a single marker repeatedly predicts recovery across taxa, stages, and stressors—would argue against the need for the proposed multilevel architecture.

Results and Discussion

The regulatory stressome reframes insect stress physiology around coordination rather than pathway accumulation. Its purpose is not to rename the collective stress response but to distinguish biological variables that are often conflated. Injury, pathway activation, repair, metabolic change, endocrine communication, and life-history output can occur in different tissues and on different timescales. Treating them as one response risks mistaking compensation for protection or molecular normalization for organismal recovery.

The evidence supporting this argument is uneven across biological levels. Heat and temperature dominate the selected literature, and *Drosophila* provides disproportionate mechanistic depth. Thermal damage–repair concepts [6] and nutrient-sensing mechanisms [16] establish useful principles, but those principles do not demonstrate conserved network structure across Insecta. Comparative endocrine evidence further shows that reproductive

regulation itself differs among insect lineages [19]. Consequently, the stressome should be parameterized separately for taxa and stages rather than populated with assumed universal pathway roles.

Laboratory-to-field transfer is another major boundary. Population-specific nutritional responses under different temperatures [20], sex-specific reproductive sensitivity [21], and developmental carry-over after predator exposure [24] all imply that environmental history and biological context can alter outcomes. Field conditions add fluctuating resources, microclimates, pathogens, pesticides, predators, and behavioral thermoregulation that are difficult to reproduce simultaneously. Compound-stressor results in honey bees [25] additionally caution that multiple exposures need not produce additive molecular responses.

Measurement design is equally important because each stressome state requires a different evidential class. Transcript abundance, antioxidant capacity, metabolite concentration, mitochondrial performance, endocrine output, tissue integrity, fertility, and survival cannot be treated as interchangeable indicators. Their relationships may strengthen, weaken, or reverse across recovery. A robust test should therefore specify which variable represents damage, which represents attempted compensation, which represents restored function, and which remains only an inferred consequence. This separation is especially important when comparing laboratory assays with ecologically variable environments, where behavior can alter realized exposure before cellular mechanisms are engaged and where repeated stress may change baseline physiological state.

The model also separates plasticity from adaptation. A response that restores short-term function may be compensatory without having been shaped as an adaptation to that particular stressor. Developmental carry-over may reflect constraint rather than anticipatory programming, and metabolic remodeling can accompany costs as well as benefits. Likewise, reproductive suppression should not automatically be called strategic reallocation when direct injury could explain the same phenotype.

Validation therefore requires experiments designed around trajectories and competing explanations. Useful studies would combine direct damage measurements with repair indicators, mitochondrial or substrate-state measures, endocrine readouts, and independent functional endpoints. Repeated sampling through recovery would help distinguish transient compensation from persistent dysfunction. Factorial manipulations could test whether modifying repair or energetic state changes downstream endocrine and life-history consequences, while cross-species replication would determine which edges are conserved and which are lineage specific.

The strongest test of the proposed stressome is therefore not whether every component can be measured, but whether explicit separation of its states improves mechanistic discrimination. If damage, repair, metabolism, endocrine coordination, and allocation repeatedly collapse onto one common trajectory, the framework is unnecessarily complex. If they decouple predictably across stress intensity, developmental stage, sex, taxon, or recovery time, then the model provides a useful structure for explaining why apparently similar exposures yield different physiological outcomes.

Conclusion

Insect stress physiology is better represented as an interaction among non-equivalent biological states than as activation of a single generalized stress response. Cellular damage can initiate signaling without being repaired; repair can consume or redirect metabolic resources; metabolic state can alter endocrine communication; and endocrine coordination can reshape life-history allocation. These relationships remain conditional on species, sex, life stage, tissue, environmental history, and timescale.

The proposed regulatory stressome organizes these distinctions into a testable molecular-physiological model while preserving the boundary between evidence-supported mechanisms and cross-level synthesis. Its central implication is methodological: recovery, compensation, and persistent dysfunction should be evaluated through coordinated trajectories across multiple levels rather than inferred from one biomarker or survival endpoint. The model will gain value only through comparative, longitudinal, and mechanistically discriminating tests that determine where its connections hold, where they differ, and where simpler explanations are sufficient.

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