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Heat, Hypoxia, Desiccation, and Immunity Interact Through Shared Molecular Pathways During Compound Physiological Stress in Insects

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ABSTRACT

Insects rarely experience heat, oxygen limitation, water loss, and immune challenge as biologically independent perturbations. Yet these stressors are often interpreted through separate pathway literatures, encouraging a one-stressor–one-response view that obscures shared demands on redox control, ATP production, substrate allocation, membrane and barrier integrity, proteostasis, repair, and endocrine-metabolic regulation. This article develops an molecular-systems model in which the four stress domains remain distinct at exposure and proximal-sensing levels but can converge on shared physiological nodes. Evidence from insect models supports specific intersections, including thermal-history effects on later hypoxia sensitivity, heat–desiccation coupling through cuticular function, dehydration-dependent modification of infection outcome, and heatwave-induced changes in immune performance. However, no current evidence establishes a universal four-stressor master pathway. The model therefore separates directly demonstrated links from cross-study synthesis and proposed network relationships. It further distinguishes molecular activation from protection, acclimatory state from evolutionary adaptation, and laboratory pathway effects from field-generalizable outcomes. The resulting architecture predicts that compound-stress phenotype should depend not only on stressor identity and intensity, but also on tissue, life stage, taxon, exposure order, recovery opportunity, and pre-existing energetic and redox state. This framework provides testable organizing principles for experiments that manipulate stress combinations while measuring shared nodes and downstream damage rather than treating each stress response as an isolated program.

Keywords: Compound stress, Insect stress physiology, HIF signaling, Redox homeostasis, Immunometabolism, Desiccation resistance.

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Introduction

The central problem in compound insect stress physiology is not simply that multiple stressors co-occur; it is that responses measured under one stressor can be misread as independent when their molecular costs and protective systems overlap. Comparative evidence shows substantial lineage-level heterogeneity in thermal tolerance and its molecular correlates, making a single conserved response topology untenable across insects [1]. A compound-stress model must therefore explain convergence without erasing taxonomic variation.

Heat tolerance itself is increasingly understood as a balance among damage, protection, and repair operating across molecular, cellular, organismal, and environmental scales [2]. This systems view is more informative than assigning tolerance to one marker such as a heat-shock protein or antioxidant enzyme. Here, that logic is extended cautiously: the existence of multilevel thermal control does not demonstrate a four-stressor network, but it establishes why shared physiological capacity must be considered when several stressors recruit overlapping maintenance systems.

Water balance forms a distinct physiological axis that can intersect climatic stress through cuticular permeability, respiratory water loss, behavior, and internal osmotic regulation [3]. It should therefore remain a separate stress origin even when it converges downstream with heat-sensitive barrier or metabolic processes. Oxygen limitation is likewise not defined by one ambient oxygen concentration. Functional hypoxia arises when oxygen supply becomes insufficient relative to tissue demand, with the threshold modified by temperature, activity, body size, development, and tracheal capacity [4]. Treating desiccation or hypoxia merely as generic “metabolic stress” would discard the causal distinctions needed to interpret compound exposure.

Immunity introduces another form of physiological demand because defense can reorganize nutrient use and endocrine signaling rather than simply adding an independent energetic cost. In *Drosophila*, immune function is tightly coupled to systemic and cellular metabolism, including insulin-related regulation and nutrient allocation [5]. The relevant inference is not that every insect uses the same immune-metabolic program, but that immunity can change the state of energetic nodes subsequently encountered by abiotic stress.

That inference has direct cellular support in *Drosophila* macrophages, where immune activation increases aerobic glycolysis and the metabolic shift is required for effective antibacterial defense in the tested system [6]. This establishes a concrete link between immune function and central carbon metabolism while remaining specific to cell type, developmental context, and antibacterial challenge. The model developed here consequently keeps heat, hypoxia, desiccation, and immunity separate at their proximal origins, then asks where their consequences converge, compete, or condition one another. Its central contribution is a proposed molecular-systems architecture that distinguishes directly supported intersections from candidate shared nodes and sequence-dependent predictions.

Heat-stress signaling

Heat stress initiates both damage and protective responses, and those processes should not be treated as synonymous. In third-instar *Drosophila*, acute heat increased heat-shock protein expression, cytosolic Ca^{2+} , and reactive oxygen species in association with cell-stress and death pathways; importantly, the tested autophagy-associated acidification readout was not activated under the same conditions [7]. This combination of positive and null findings argues against converting any single stress marker into a universal index of successful thermal protection. Acclimation effects were also condition dependent, reinforcing that prior state modifies acute signaling.

Heat-shock proteins provide a clearer example of pathway involvement, but their interpretation still depends on the outcome measured. Experimental work in *Drosophila* links specific HSP responses to temperature-stress-associated apoptosis [8]. Such findings support a role for chaperone systems in controlling the balance between damaged-protein burden and cell survival, but they do not imply that HSP induction is sufficient to prevent injury in every tissue or taxon.

The same boundary applies across species. In *Bombyx mori*, HSP19.9 and HSP90 participate in experimentally measured heat-stress responses [9]. These molecular responses are evidence of stress handling in a lepidopteran model, not evidence that an identical chaperone program is universal or that inducibility itself demonstrates evolutionary adaptation. For the proposed systems model, HSP activity is therefore represented as a conditional proteostasis resource rather than a taxon-invariant thermal switch.

Thermal exposure can also reach structural pathways not traditionally placed at the center of heat signaling. Multi-omics analysis in *Spodoptera frugiperda* identified chitin-related molecular changes during high-temperature response [10]. Because chitinous and cuticular structures also influence water exchange, this finding creates a plausible interface between thermal stress and barrier biology. The evidence, however, supports heat-associated structural remodeling in this species; it does not by itself establish that heat and desiccation share an identical cuticular mechanism.

Functional manipulation strengthens the case that particular chaperones can be protective in defined systems. Overexpression of Bmhs19.9 improved high-temperature outcomes in *Bombyx* cells and transgenic silkworms

[11]. That intervention supports a causal protective role for this protein under the tested conditions, while its engineered expression and species specificity limit transfer to endogenous variation in other insects. The distinction matters because a systems model should weight manipulated pathway evidence more strongly than expression correlation without mistaking it for universality.

Redox signaling is another recurrent thermal response, yet its evidential status is often overstated. Across insect studies, heat commonly alters antioxidant systems, whereas direct evidence that antioxidant induction prevents oxidative biomolecular damage remains comparatively limited; evidence linking heat exposure itself to measured ROS production is also uneven [12]. Accordingly, the proposed model treats redox regulation as a shared candidate node with an explicit boundary between antioxidant response, oxidative damage, and demonstrated protection.

Hypoxia signaling

Hypoxia adds a different proximal constraint: oxygen supply becomes inadequate relative to demand. Even so, its phenotype can depend on previous thermal conditions. In *Drosophila*, developmental and evolutionary thermal histories altered later sensitivity to paralyzing hypoxia, with interactive rather than uniformly monotonic effects [13]. This provides direct evidence that one environmental history can modify a later response to another stress domain, while leaving open whether cell size, developmental remodeling, metabolic state, or additional correlated traits mediate the effect.

At the signaling level, hypoxia-inducible factor activity is strongly context dependent. In the *Drosophila* prothoracic gland, HIF signaling regulates growth and development under hypoxia but is not required for the corresponding control under normoxia [14]. The contrast is important for compound-stress reasoning: HIF should not be represented as a constitutively dominant regulator merely because it is central under oxygen limitation. Oxygen state, tissue, and developmental stage define the boundary of the demonstrated mechanism.

One downstream consequence is metabolic reprogramming. *Drosophila* HIF-1 α /Sima is functionally required for establishment of the larval glycolytic program [15]. This makes glycolysis an evidence-based energetic intersection for the model, but only at the appropriate level of inference. It does not establish that all stress-induced glycolysis in insects is HIF dependent, nor that increased glycolytic flux necessarily improves tolerance under simultaneous heat, water loss, or immune activation.

Hypoxia tolerance can also depend on organ-specific mitochondrial metabolism. Renal L-2-hydroxyglutarate dehydrogenase activity supports hypoxia tolerance and mitochondrial metabolism in *Drosophila* [16]. Such evidence cautions against collapsing “energy metabolism” into a homogeneous whole-organism node: tissue-specific metabolite handling may determine whether systemic oxygen limitation is buffered or amplified.

Transcriptional regulation is similarly modular. Functional promoter analysis identified CmZFH as a co-regulator of particular hypoxia-responsive genes in the tested insect system [17]. The result supports gene-specific regulatory architecture beyond a single canonical HIF axis. In the proposed network, hypoxia signaling therefore contains modular transcriptional branches rather than a universal linear cascade.

At severe oxygen deprivation, energetic disturbance couples directly to broader homeostasis. In *Locusta migratoria*, anoxia disrupted ATP status together with water, ion, and acid–base balance, and recovery revealed the temporal coupling of these disturbances [18]. Because anoxia is an extreme oxygen condition, its magnitude should not be transferred to ordinary hypoxia. Nevertheless, the study demonstrates that oxygen failure can propagate across energy and water/ion regulation, providing a mechanistic reason for cross-stressor interactions when those same systems are already challenged.

Hypoxia also alters developmental coordination rather than acting only through acute ATP limitation. In *Drosophila*, hypoxia delayed steroid-induced developmental maturation through suppression of EGF signaling [19]. This establishes a developmental signaling consequence in a defined larval context. For the broader model, developmental stage must therefore be treated as both a modifier of stress response and a possible downstream target, rather than as background metadata.

Desiccation responses

Desiccation begins with water-balance failure, but its molecular consequences extend into barrier structure and metabolism. In *Plutella xylostella*, a cuticular protein contributed functionally to both thermal and desiccation tolerance through barrier and water-homeostasis processes [20]. This is unusually direct evidence for a heat–

desiccation intersection. It supports a shared structural/homeostatic route in this lepidopteran system, not a claim that the cuticle is the sole or universal bridge between the two stressors.

Cuticular chemistry itself contains separable mechanisms. In *Blattella germanica*, desiccation resistance was linked to tanning-related processes and calcium-associated molecular responses, with Laccase-2 important to cuticle tanning and survival in the tested system [21]. These findings justify keeping barrier hardening and calcium/ion-linked responses analytically distinct: their co-occurrence does not establish a single calcium-controlled desiccation program across insects.

Water loss also changes fuel use. In *Ceratitis* fruit flies, desiccation and recovery were accompanied by flexible nutrient oxidation associated with differences in climate-stress resistance [22]. This makes substrate availability and oxidation plausible determinants of the energetic state carried into a subsequent stress. The result does not identify one optimal fuel-switching rule, and its transfer is constrained by species, nutrient condition, exposure duration, and recovery phase.

Functional evidence further supports the importance of lipid barrier construction. Silencing a fatty acyl-CoA reductase in *Locusta migratoria* disrupted the lipid-based cuticle barrier [23]. The experiment demonstrates that a defined lipid-biosynthetic component can be required for barrier integrity in this species, but it cannot establish that the same enzyme controls desiccation tolerance across insects. In systems terms, cuticular lipids represent one mechanistic route by which energetic substrate allocation can influence water-loss defense.

Exposure regime adds another layer of conditionality. In ants, cuticular hydrocarbon acclimation differed among species and between constant and fluctuating climatic treatments [24]. Mean temperature or humidity therefore cannot always substitute for experienced temporal structure. This evidence is especially important for later sequence predictions because a prior exposure may modify barrier phenotype without producing the same state as an equivalent constant exposure.

Immune activation

Immune activation is not simply an additional drain on a fixed energy pool; it can actively reconfigure allocation. In *Drosophila*, JAK/STAT-mediated insulin resistance in muscle was required for an effective immune response in the tested context [25]. The result directly connects immune signaling with systemic metabolic redistribution. It does not justify treating insulin resistance as universally beneficial, because its value depends on infection state, tissue, duration, and the costs imposed on other physiological functions.

Host–microbe context further changes the meaning of “immune activation.” *Drosophila* control of an endosymbiont can involve non-canonical immune signaling coupled to gut metabolic remodeling [26]. This differs biologically from acute pathogen clearance even though both engage defense-associated signaling. A compound-stress model must therefore distinguish pathogen defense, microbiota or symbiont control, and sterile immune activation rather than treating all immune states as metabolically equivalent.

Canonical immune pathways can also act through endocrine interfaces. The *Drosophila* IMD pathway modulates enteroendocrine function and systemic host metabolism [27]. This provides a route by which local gut immune signaling may alter whole-organism nutrient allocation. The evidence supports that relationship in a defined *Drosophila* gut context; it does not establish that every insect immune pathway produces the same endocrine-metabolic state.

Crucially, direct cross-stressor evidence exists for hydration state. In *Aedes aegypti*, dehydration-induced regulation of Ae-Aper50 altered midgut infection outcome [28]. This demonstrates that dehydration-responsive molecular regulation can change an infection-related phenotype in a specific mosquito–midgut system. It does not establish a universal direction—suppression or enhancement—of immunity under desiccation, because pathogen identity, tissue, dehydration protocol, and vector physiology constrain the inference.

Thermal–immune interaction is likewise endpoint dependent. A simulated natural heatwave altered bumblebee immune measures and resistance to infection [29]. The study establishes that thermal history can perturb host defense under an ecologically motivated heat regime, while different immune components and infection outcomes need not move in the same direction. Together with the dehydration evidence, it shows why compound stress cannot be inferred from adding single-stressor response magnitudes: one stressor may alter the state of the pathways through which another challenge is expressed.

The distinction between immune signaling, metabolic reallocation, and cross-stressor modification is easier to recover when the evidence is organized by mechanism and boundary rather than by a single “immune cost”

category. **Table 1** therefore separates directly observed immune–metabolic states from the more limited pairwise evidence that dehydration or heat can modify infection-related outcomes.

Table 1. Immune-state mechanisms and evidential boundaries governing entry of immune activation into compound physiological stress

Interface	Evidence frame	Compound-stress meaning	Boundary and test
Mechanistic immune–metabolic interfaces			
	Biological context	Interpretation for compound stress	Boundary or uncertainty
JAK/STAT-linked muscle insulin resistance	<i>Drosophila</i> ; systemic muscle–immune interaction	Immune challenge can redistribute metabolic resources through endocrine control	Infection-, tissue-, duration-, and species-specific; not inherently beneficial outside the tested state
	Observable or evidential basis Immune effectiveness depends on induced insulin-resistance signaling in muscle	Status Evidence-supported mechanism; broader convergence proposed	Research/test implication Measure insulin signaling and resource allocation alongside defense outcomes under added abiotic stress
	Biological context	Interpretation for compound stress	Boundary or uncertainty
Non-canonical defense with gut metabolic remodeling	<i>Drosophila</i> host–endosymbiont interaction	Host–microbe regulation can alter the metabolic background on which abiotic stress acts	Symbiont control is not equivalent to pathogen clearance or sterile activation
	Observable or evidential basis Microbial control occurs with coupled immune signaling and metabolic remodeling	Status Evidence-supported context; cross-stressor extension proposed	Research/test implication Separate microbial relationship type when testing energetic consequences of immunity
	Biological context	Interpretation for compound stress	Boundary or uncertainty
IMD–enteroendocrine coupling	<i>Drosophila</i> gut and systemic metabolism	Local immune activity can propagate to organismal nutrient-allocation state	Pathway, tissue, microbiota, and species boundaries limit generalization
	Observable or evidential basis Canonical immune signaling modifies enteroendocrine function and host metabolism	Status Evidence-supported mechanism; systems role proposed	Research/test implication Pair gut immune readouts with endocrine and whole-organism metabolic measurements
Direct pairwise stress modifiers			
	Biological context	Interpretation for compound stress	Boundary or uncertainty
Dehydration-responsive infection modulation	<i>Aedes aegypti</i> midgut infection system	Hydration state can directly modify an infection-related molecular phenotype	Direction cannot be generalized across pathogens, tissues, or insects
	Observable or evidential basis Dehydration-induced Ae-Aper50 regulation changes infection outcome	Status Direct pairwise interaction	Research/test implication Manipulate hydration and infection factorially while measuring the implicated molecular route
	Biological context	Interpretation for compound stress	Boundary or uncertainty
Heatwave-associated immune perturbation	Bumblebee heatwave and infection context	Thermal history can alter host-defense phenotype	Immune endpoints may diverge; one heatwave design does not define a universal thermal effect

Observable or evidential basis	Status	Research/test implication
Simulated heatwave changes immune measures and infection resistance	Direct pairwise interaction	Use multiple immune endpoints and infection outcomes across realistic thermal histories

Shared redox and energetic nodes

The strongest basis for a shared-stress architecture is not a universal marker but convergence on redox and energetic control under different experimentally defined conditions. In *Tribolium castaneum*, HIF-1 α contributes functionally to antioxidant regulation during hypoxia [30]. This provides a direct hypoxia–redox connection in a beetle, while species, oxygen regime, tissue, and antioxidant endpoint constrain transfer. It does not establish HIF-1 α as the common redox controller of heat, desiccation, and immunity.

Redox enzymes can also influence immune-state biology. Peroxiredoxins regulate aspects of immunity and aging in *Drosophila* [31], demonstrating that antioxidant systems can participate in defense rather than merely detoxify damaging oxidants. Conversely, mitochondrial perturbation in *Drosophila* immune cells enhanced cell-mediated innate immunity under the tested conditions [32]. Mitochondrial disturbance therefore cannot be interpreted monotonically as immune failure; organelle state, perturbation severity, and cell type determine the direction of the response.

Energetic convergence is similarly conditional. HIF-dependent glycolytic programming in *Drosophila* larvae [15], simultaneous disruption of ATP and water/ion/pH balance during locust anoxia [18], and immune-driven JAK/STAT–insulin reallocation [25] each show that central energy state can be reorganized by different stress domains. Desiccation-associated nutrient oxidation [22] and heat-linked antioxidant responses [12] add further routes into this field. The proposed synthesis is therefore a shared redox–energy state space, not a master pathway: upstream triggers remain distinct, while ATP availability, mitochondrial state, substrate allocation, and redox regulation can become common constraints.

Figure 1 shows the central topological distinction: directly supported stress-to-node relationships remain visible while proposed cross-stressor convergence and transfer boundaries are kept separate.

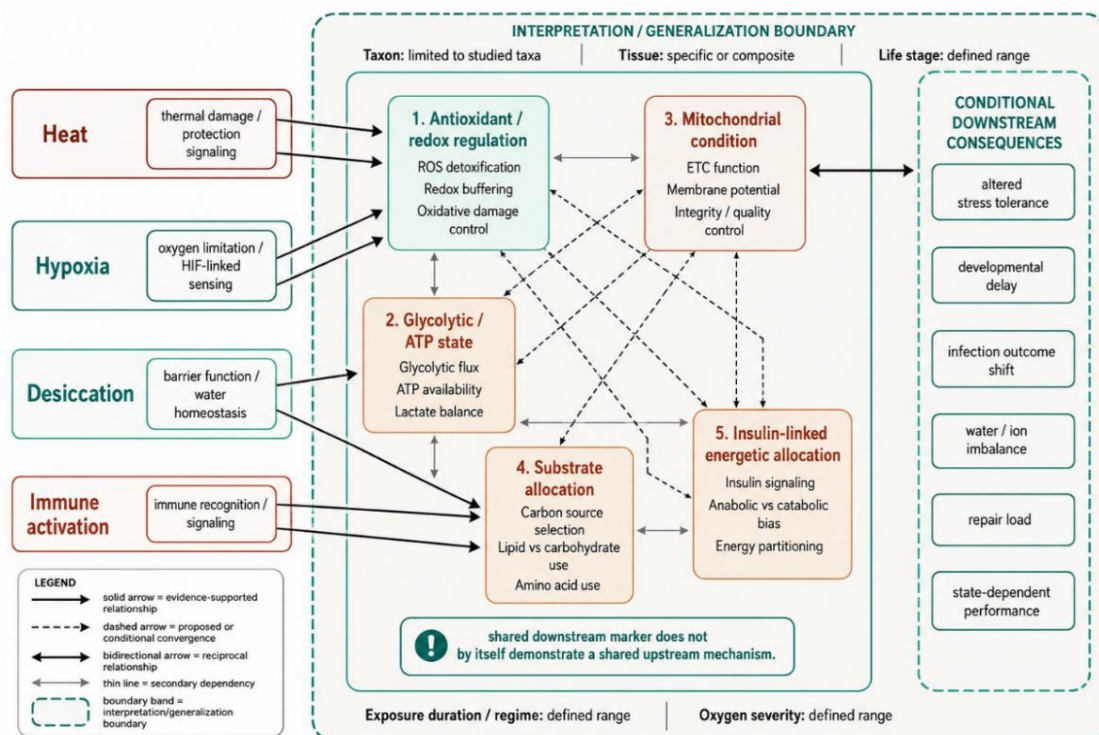


Figure 1. Redox–energy convergence across four stress domains with explicit evidence and transfer boundaries

Proteostasis and repair crosstalk

Proteostasis is a plausible cross-stressor interface, but the evidence is less complete than the redox–energy case. At arthropod pathogen–vector interfaces, cellular stress programs including unfolded-protein and integrated-stress responses intersect with immunity, although many mechanistic links remain conditional or incompletely resolved [33]. They therefore cannot be assigned the role of a proven coordinator of all four focal stresses.

Heat provides direct evidence for the distinction between proteotoxic demand, repair, and terminal injury. Acute heat in *Drosophila* larvae co-occurred with HSP induction, ROS and Ca^{2+} -linked stress, while the tested autophagy readout was not activated [7]. By contrast, engineered Bmhsp19.9 overexpression improved thermal outcomes in *Bombyx* [11]. Chaperone capacity can thus be protective in a defined system without making HSP induction synonymous with successful repair.

Mitochondrial perturbation can enhance innate immune-cell function in *Drosophila* [32], further showing that cellular stress signaling and functional outcome need not have a simple negative relationship. The proposed crosstalk architecture consequently separates proteotoxic burden, protective chaperoning, organelle stress, and immune consequence.

Table 2 keeps these cross-scale states from being collapsed into a single “stress response,” particularly where evidence moves from molecular perturbation to cellular or organismal interpretation.

Table 2. Proteostasis–repair states that delimit molecular crosstalk under compound insect stress

Evidence dimension	Proteotoxic burden with cell-injury signaling	Protective chaperone capacity	Stress-response/immune interface	Mitochondrial stress with altered immune function
Scale and biological context	<i>Drosophila</i> larval heat response	<i>Bombyx</i> cells and transgenic silkworm	Arthropod pathogen–vector systems	<i>Drosophila</i> immune cells
Observable/evidential basis	HSP, ROS and Ca^{2+} -linked stress coexist with cell-death pathways	Increased Bmhsp19.9 expression improves tested thermal outcomes	Proteostasis-related stress programs intersect with immune signaling	Mitochondrial perturbation enhances cell-mediated innate immunity
Interpretation for compound stress	Protection and injury can be active simultaneously	Chaperone capacity can shift heat-response outcome	Repair pathways may condition infection-related physiology	Organelle perturbation need not equal functional failure
Boundary or uncertainty	Acute laboratory heat; tested autophagy readout was not activated	Engineered overexpression; single species	Mechanistic support varies among pathways, tissues, and vectors	Direction depends on cell type and perturbation severity
Research/test implication	Measure damage and repair endpoints separately	Test endogenous regulation and costs under combined stress	Resolve pathway-specific causality before cross-stressor transfer	Test dose, tissue, and whole-organism consequences
Status	Evidence-supported state; compound extension proposed	Evidence-supported protection; broader role proposed	Conditional evidence	Evidence-supported context; reciprocal systems role proposed

Compound-stress network

The evidence does not establish one experimentally validated pathway combining all four stressors. Instead, it establishes limited direct intersections embedded in a larger set of candidate shared nodes. A cuticular protein can influence both thermal and desiccation tolerance in *Plutella* [20]. Dehydration-responsive regulation can alter mosquito midgut infection outcome [28], while a simulated heatwave can change bumblebee immune measures and infection resistance [29]. These pairwise findings warrant connection, but not mechanistic fusion.

The proposed compound-stress network therefore has three evidential layers. First are stress-specific proximal processes: thermal damage/protection, oxygen sensing, water-balance/barrier regulation, and immune recognition/signaling. Second are experimentally supported intersections such as HIF-linked glycolysis [15], redox regulation, barrier–water homeostasis, and immune-metabolic reallocation. Third are dashed, explicitly

proposed cross-stressor links where different literatures converge on ATP demand, mitochondrial state, redox control, substrate use, or repair capacity without having tested the same compound exposure.

A key constraint is that convergence does not imply interchangeability. Barrier failure can increase water loss without passing through the same proximal regulators as hypoxia-induced glycolytic programming, and immune-driven metabolic reallocation can alter substrate availability without reproducing the signaling architecture of starvation or desiccation. The model therefore predicts interaction only when two stresses recruit, deplete, or modify a common state variable sufficiently to alter the second response. Where two pathways merely share a downstream marker, such as ROS-associated signaling, common measurement alone is insufficient evidence of a common mechanism. This distinction prevents the network from becoming a catalogue of stress-responsive molecules.

Network state is also history dependent. Thermal developmental history can modify subsequent hypoxia sensitivity in *Drosophila* [13], so prior state enters the architecture as a modifier rather than a deterministic arrow. Taxonomic heterogeneity in thermal vulnerability and molecular correlates [1] further requires an external generalization boundary. The model is therefore a falsifiable organizing structure: failure of a proposed shared node to mediate interaction under factorial exposure would narrow, rather than invalidate, the stress-specific mechanisms already supported.

Sequence-dependent predictions

Sequence dependence should be treated as a testable property of state transitions, not as automatic cross-protection. Prior anoxia exposure can buffer aspects of later anoxia stress in the soil-pupating fly *Anastrepha suspensa*, with stage-dependent effects [34]. This demonstrates physiological history within one stress class, not a general rule that prior stress is beneficial.

Cross-stressor history is supported more narrowly by thermal developmental conditions altering later hypoxia sensitivity in *Drosophila* [13]. Temporal patterning also matters for barrier phenotype: ant cuticular hydrocarbons respond differently under constant and fluctuating climatic conditions [24]. These findings motivate the proposed prediction that order, interval, and recovery can alter the state presented to a later stressor, but they do not specify a universal direction.

The proposed sequence logic yields three falsifiable outcome classes. A prior stress may prime a shared protective capacity, may deplete or damage that capacity and thereby sensitize the insect, or may leave the later response unchanged because the challenges remain mechanistically separate at the relevant scale. Recovery time can reverse an expected direction by permitting repair, substrate replenishment, barrier remodeling, or immune resolution. Consequently, a sequence effect should be assigned only when the response to the second challenge differs from an appropriate single-stressor control and when competing explanations such as developmental delay or cumulative exposure are evaluated.

Two direct pairwise cases define especially useful tests. Heatwave exposure can alter bumblebee immune and infection outcomes [29], and dehydration-responsive regulation can modify *Aedes* midgut infection [28]. Accordingly, heat→immune and dehydration→infection sequences should be tested with reciprocal order, simultaneous exposure, and recovery treatments rather than assumed to reproduce single-stressor effects. Mechanistically, experiments should measure candidate shared nodes together with stress-specific markers so that sequence effects can be distinguished from cumulative injury, developmental remodeling, pathogen timing, or resource depletion.

A rigorous validation program would factorially vary stress order, intensity, interval, and recovery while resolving tissue, life stage, sex, and taxon. Field transfer additionally requires realistic fluctuation and co-occurrence. These are proposed predictions and validation requirements; the present model supplies neither effect magnitudes nor prospective predictive accuracy.

Conclusion

Compound physiological stress in insects is best represented as distinct stress origins converging conditionally on limited shared molecular and physiological capacities. The evidence supports particular heat–desiccation, dehydration–infection, thermal-history–hypoxia, and heat–immunity intersections, while redox regulation, energetic allocation, mitochondrial state, and proteostasis provide plausible shared domains whose cross-stressor integration remains only partly tested.

The proposed molecular-systems model therefore replaces an additive one-stressor logic with an evidence-bounded state framework. Its central claim is not that insects possess one universal compound-stress pathway, but that stress order and context can change the shared physiological state through which subsequent challenges are expressed. Testing that claim requires factorial, tissue-resolved and taxonomically replicated experiments that separate pathway activation, protection, damage, and organismal consequence.

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