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Biochemical basis of insecticide resistance in agricultural insects

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Abstract

Insecticide resistance in agricultural insect pests rarely reflects the action of a single gene or a single enzyme. Populations exposed to repeated chemical selection typically accumulate several independent biochemical changes at once, and the resulting phenotype is better understood as a layered outcome than as the signature of one dominant pathway. The bioassay data, enzyme-activity assays and molecular genotyping studies on major agricultural pests, including aphids, whiteflies, lepidopteran defoliators, mites and dipteran flies, to examine how metabolic detoxification through esterases, cytochrome P450 monooxygenases and glutathione S-transferases interacts with target-site mutations affecting acetylcholinesterase, the voltage-gated sodium channel, the GABA-gated chloride channel and nicotinic acetylcholine receptors. Particular attention is paid to instances where reported resistance ratios diverge sharply between studies of the same species and insecticide, a pattern traced here to differences in assay substrate, reference strain and sampling season rather than to any inherent instability of the resistance trait itself. Reduced cuticular penetration, behavioural avoidance and emerging evidence for microbiome-assisted detoxification are treated as contributing mechanisms rather than standalone explanations.

Keywords: Insecticide resistance; metabolic detoxification; cytochrome P450 monooxygenase; target-site mutation; knockdown resistance; resistance management

1. Introduction

The definition offered by the World Health Organization more than six decades ago still frames how entomologists talk about the problem, an inherited capacity in a pest population to tolerate a dose of toxicant that would kill most individuals of a normal, unselected population of the same species (WHO, 1957). What has changed since then is the scale of the phenomenon. The first confirmed case of an insect population failing to respond to a control chemical, the San Jose scale reacting poorly to lime sulphur, dates to 1914, and only a further eleven cases had accumulated by the mid-1940s (Simon, 2014) ^[26]. DDT resistance in houseflies and in *Culex* mosquitoes, reported within three years of the compound's wartime introduction, marked the point at which resistance stopped being a curiosity and became a recurring cost of chemical control (Sacca, 1947). By the middle of the twentieth century's second half, several hundred species carried documented resistance to at least one active ingredient, and current estimates place the figure at well over five hundred, spanning organochlorines, organophosphates, carbamates, pyrethroids, neonicotinoids and, increasingly, the diamide and butenolide chemistries introduced as replacements for older classes (Simon, 2014) ^[26].

Myzus persicae occupies an unusual position, the sheer breadth of chemistries it has neutralised, more than seventy active ingredients by some counts, makes it something close to a working catalogue of every resistance mechanism known in agricultural insects (Silva *et al.*, 2012) ^[26]. Its life history, rapid parthenogenetic turnover, a wide host range and strong dispersal through winged morphs, gives selection pressure many generations in which to act each season, and this alone goes some way toward explaining why the species keeps reappearing across the review literature on resistance mechanisms.

Four broad categories are conventionally used to organise the biochemistry of resistance, enhanced metabolic detoxification, target-site insensitivity, reduced cuticular penetration and behavioural avoidance (Hemingway & Ranson, 2000; Bass & Field, 2011) ^[15, 3]. French-

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Constant (2013) ^[13] argued that the molecular genetics underlying each category converge on the same basic evolutionary logic, a mutation or regulatory change that alters either the amount or the specificity of a protein, and Bass *et al.* (2015) ^[3] showed for neonicotinoid resistance specifically that metabolic and target-site changes are found together far more often than either is found alone. Sparks and Nauen (2015) ^[27] made the practical case for organising insecticide rotation programmes around the IRAC mode-of-action classification precisely because single-mechanism assumptions have repeatedly failed as a working basis for resistance management. Van Leeuwen and Dermauw (2016) ^[31], writing on chelicerate mites rather than insects, reached much the same conclusion from a different taxonomic angle, that xenobiotic metabolism genes expand and diversify under selection in ways that make prediction from a single species' resistance profile unreliable.

2. Metabolic Detoxification and the Enzymatic Architecture of Resistance

Esterase-mediated sequestration remains the most thoroughly documented metabolic pathway in agricultural pests, and the aphid literature illustrates why. Gene amplification at the *E4* and *FE4* loci in *Myzus persicae* produces esterase titres many times greater than in susceptible clones, and resistant individuals have been shown to carry between five and eleven times more copies of the relevant esterase gene sequences than unselected populations (Khan *et al.*, 2020) ^[18]. This amplification is not always accompanied by a proportional rise in the resistance ratio measured against a given insecticide, a mismatch that becomes clearer once enzyme-activity assays are compared directly with whole-organism bioassay results. Zhu and Snodgrass (2004) ^[35], working on the tarnished plant bug, found that the same resistant strain returned a three-fold, a six-fold or a ten-fold difference from the susceptible reference depending only on which chromogenic substrate, alpha-naphthyl acetate, beta-naphthyl acetate or p-nitrophenyl acetate, was used in the microplate assay. Read narrowly that spread could look like inconsistent biology; read correctly it says something about the assay rather than about the insect, since each substrate probes a different subset of the esterase pool and none functions as a universal proxy for whole-body detoxification capacity.

Cytochrome P450 monooxygenases occupy a comparable position in the pyrethroid and neonicotinoid resistance literature, and the regulatory route to over-expression differs in an important way from the esterase story. Where esterase resistance is frequently traced to outright gene amplification, P450 up-regulation more often arises from changes in cis-regulatory sequence or transcription-factor activity rather than from additional gene copies (Khan *et al.*, 2020) ^[18]. Hu *et al.* (2023) ^[16] reported a Chinese field population of *Myzus persicae* carrying resistance ratios of 106.9 for imidacloprid and 324 for beta-cypermethrin, attributing both to metabolic mechanisms rather than to a single target-site change, a scale of resistance that a purely gene-dosage model of detoxification struggles to explain on its own. Shi *et al.* (2016) ^[24], working with the carmine spider mite, found that the recombinant TCE2 carboxylesterase produced roughly double the specific activity of the crude susceptible extract, a comparatively modest fold-difference given the magnitude of whole-organism resistance ratios reported.

Glutathione S-transferases round out the three principal detoxification families, acting mainly through conjugation of reduced glutathione to electrophilic insecticide metabolites rather than through direct hydrolysis or oxidation (Khan *et al.*, 2020) ^[18]. Zhu and Luttrell (2015) ^[34], examining altered gene regulation in the tarnished plant bug, noted that transcriptional changes across several detoxification gene families tend to move together under imidacloprid selection rather than one family compensating in isolation, a finding difficult to reconcile with resistance-management schemes built around a single enzyme class.

3. Target-Site Insensitivity and the Genetics of Reduced Binding Affinity

Target-site insensitivity works through a different logic from metabolic detoxification, changing the shape or charge of the binding pocket rather than the quantity of insecticide reaching it, and the molecular targets involved map closely onto the neural physiology each insecticide class was designed to disrupt. Modified acetylcholinesterase and the sodium-channel *kdr* and super-*kdr* mutations remain the best characterised examples, but four field surveys published between 2022 and 2024 show how much finer-grained the genotyping has become. Daum *et al.* (2024) ^[10] sampled oilseed rape weevils across French and German fields and found the L1014F *kdr* mutation ranging from complete absence to fixation depending on the population, with homozygote frequency above fifty-five percent corresponding closely to documented pyrethroid control failure at the recommended field rate, while populations below roughly twelve percent homozygosity remained controllable. That dose-response relationship between genotype frequency and observed control outcome is one of the few instances in a single molecular marker tracks field performance closely enough to be used as a stand-alone monitoring tool.

Other *kdr* surveys complicate that picture rather than reinforcing it. Zhang *et al.* (2024) ^[14] documented both the M918T and L1014F substitutions together in *Lygus pratensis* from Inner Mongolia, with combined homozygous and heterozygous genotypes reaching sixty percent of sampled individuals in populations already showing high resistance to lambda-cyhalothrin, a co-occurrence of two target-site changes in the same channel that raises the question of whether either mutation alone would have produced comparable field resistance. Valmorbidia *et al.* (2022) ^[30] found the L1014F and M918I combination in pyrethroid-resistant soybean aphid and used the pairing to design PCR-based markers for surveillance, while Gao *et al.* (2024) ^[14] went further, functionally confirming through heterologous expression that a double mutation, T929I paired with K1774N, reduces pyrethroid-induced sodium current in field-resistant bean flower thrips from Hainan Province. Read together, these four studies suggest that single point mutations are becoming the exception rather than the rule in newly surveyed pyrethroid-resistant populations, a trend consistent with the earlier observation in Colorado potato beetle that *kdr* resistance has arisen independently through multiple distinct mutational routes within the same species rather than spreading from one ancestral origin (Rinkevich *et al.*, 2012; Dong *et al.*, 2014) ^[20, 12].

Nicotinic acetylcholine receptor mutations follow a comparable pattern in aphids. Bass *et al.* (2011) ^[4] traced

neonicotinoid resistance in *Myzus persicae* to a single point mutation in the D-loop region of the M μ B1 receptor subunit, and this discovery gave the field one of its clearest single-gene markers for a chemistry class introduced relatively recently, though the same species' broader resistance profile makes clear that this mutation rarely operates in isolation from metabolic changes occurring at the same time.

Acetylcholinesterase insensitivity, the mechanism underlying much organophosphate and carbamate resistance, illustrates the limits of assuming target-site involvement wherever whole-organism bioassays show resistance. Tiwari *et al.* (2012) ^[29] measured AChE activity across laboratory and field populations of the Asian citrus psyllid and found overlapping ranges between the two, a result that led the authors to rule out target-site insensitivity as the basis for the organophosphate and carbamate resistance they had already confirmed through dose-mortality assays. Alvi *et al.* (2012) ^[2], studying field-evolved *Helicoverpa armigera* resistant to cypermethrin at ratios reaching nearly two thousand-fold in Pakistan, attributed the extreme scale of that resistance to kdr-type sodium channel mutation acting together with elevated cytochrome P450 activity rather than to either mechanism working alone, a resistance ratio an order of magnitude beyond what either mechanism produces independently.

4. Cuticular, Behavioural and Microbiome-Associated Contributions

Reduced cuticular penetration rarely produces resistance on its own, but its effect is to buy time for the enzymes described above, and this synergistic role is probably why it receives less standalone research attention than metabolic or target-site mechanisms despite being reported across a wide taxonomic range. DDT-resistant tobacco budworm larvae carry a cuticle with a higher proportion of protein and lipid and a greater degree of sclerotisation than susceptible larvae, slowing the rate at which the toxicant reaches the haemolymph even though it eventually does so (Saha, 2016) ^[22]. *Musca domestica* shows a related pattern, resistant strains carrying higher total lipid, monoglyceride, fatty acid, sterol and phospholipid content in the cuticle than susceptible strains (Saha, 2016) ^[22], and because this thickening slows penetration against a broad range of insecticide chemistries rather than one specific class, cuticular resistance tends to appear alongside, and to amplify, whichever metabolic or target-site mechanism a given population has already acquired.

Behavioural resistance operates on an entirely different timescale, altering exposure before the insecticide contacts the cuticle at all rather than after. Mosquitoes that avoided resting on DDT-treated surfaces long enough to absorb a lethal dose, and carbaryl-resistant fall armyworm larvae that recognised and refused to feed on treated leaf surfaces, are among the older documented cases, and a more unusual example comes from fenvalerate-exposed *Plutella xylostella* populations that shed the affected metathoracic leg on tarsal contact with residue, a phenomenon termed leg autotomy (Simon, 2014) ^[26]. Colorado potato beetle populations facing repeated foliar spraying have similarly been observed shifting toward the undersides of leaves or reducing overall feeding activity, and diamondback moth populations under sustained insecticide pressure have reduced oviposition on treated crop surfaces (Thenmozhi & Chandrakar, 2026) ^[28]. None of these behavioural shifts requires a change in

enzyme activity or receptor structure, which is precisely why they are difficult to detect through the biochemical and molecular assays that dominate the resistance-monitoring toolkit, and why bioassay data collected without any behavioural observation component risk under-estimating a population's true field performance.

A less conventional line of evidence has emerged around microbiome contributions to detoxification capacity, and while this mechanism sits outside the four-category framework used through most of this review, it is increasingly difficult to set aside. Populations of the cotton aphid *Aphis gossypii* resistant to imidacloprid carry a higher relative abundance of the gut symbiont *Sphingomonas*, a genus with demonstrated capacity to metabolise insecticide compounds directly, than susceptible populations, while sub-lethal imidacloprid exposure in the brown planthopper *Nilaparvata lugens* increases *Wolbachia* abundance, which in turn raises host cytochrome P450 activity (Thenmozhi & Chandrakar, 2026) ^[28]. Whether these symbiont associations represent a stable, heritable component of resistance or a more transient, exposure-induced state remains an open question, and the agricultural pest literature has not yet produced the multi-generation tracking data needed to settle it.

5. Quantifying Resistance, Assay Dependence and the Problem of Field Variability

Nowhere is the gap between reported numbers and underlying biology clearer than in the resistance-ratio literature for *Bemisia tabaci* and imidacloprid, a pest-insecticide pairing studied more intensively than almost any other in this review. Byrne *et al.* (2003) ^[7] reported ratios of fifty-eight to one hundred and twenty-six fold in Guatemalan B-biotype populations; Schuster *et al.* (2010) ^[23], monitoring Florida populations across eight consecutive years, recorded a much lower range of 3.7 to 26.3 fold; and Khalid *et al.* (2021) ^[17], working from laboratory selection over five generations, obtained an intermediate figure of eighty-six fold. Read as a single data point each of these studies would suggest a fairly stable, well-defined level of imidacloprid resistance in this whitefly, yet placed side by side the three figures span more than a thirty-fold range for what is nominally the same resistance phenotype in the same species. Geography, selection history and, most importantly, the identity of the susceptible reference strain used as the denominator in each ratio calculation all move independently of the pest's actual biochemistry, and a resistance ratio is consequently best treated as a property of the measurement system as much as of the population being measured.

The Florida monitoring dataset adds a further complication that a snapshot resistance ratio cannot capture, its trajectory over time. Schuster *et al.* (2010) ^[23] found RR50 values for imidacloprid falling from 12.0 in 2003 to 2.5 in 2005 before climbing back to 26.3 by 2006, a non-monotonic pattern inconsistent with the simple assumption that resistance, once it appears, only accumulates further under continued selection. The same dataset showed resistant sub-populations reared for six generations without imidacloprid exposure reverting from RR50 values of fifty to sixty down to four or below, evidence for a fitness cost attached to the resistance allele that only becomes visible once selection pressure is relaxed. For resistance-management planning this carries a direct and somewhat counter-intuitive

implication, rotation intervals need to run long enough to allow that reversion to occur, since a rotation cycled too quickly back to imidacloprid will reintroduce selection before the susceptible genotype has had a chance to recover ground in the population.

The acaricide literature shows an even wider spread. Díaz-Arias *et al.* (2019) ^[11] reported abamectin resistance ratios of 2,226 to 21,141 fold in a Mexican field population of *Tetranychus urticae* associated with cut roses, a range that dwarfs every insecticide resistance ratio quickly resistance can escalate in a species combining short generation time, high fecundity and repeated exposure to a single acaricide class under intensive greenhouse production. Set against the *Diaphorina citri* case, where Tiwari *et al.* (2012) ^[29] found no separation at all between resistant and susceptible AChE activity despite confirmed field resistance, the acaricide and psyllid data together make the same point from opposite directions, that the magnitude and even the mechanistic basis of resistance in one pest-insecticide system carries almost no predictive value for another, and extrapolating a resistance ratio or a mechanism from a well-studied species to a poorly studied relative is a weaker inference than the review literature sometimes implies.

6. Detection Gaps, Monitoring Limitations and Emerging Management Options

Three broad detection strategies dominate current practice, whole-organism dose-mortality bioassay, biochemical microplate assay of enzyme activity, and molecular diagnostics targeting known point mutations, and each carries a distinct blind spot rather than a shared one. Bioassays capture the net phenotype regardless of mechanism but say nothing about which biochemical pathway produced it. Biochemical assays, as the *Lygus lineolaris* substrate comparison demonstrates, are sensitive to the specific chromogenic substrate chosen and can generate several-fold different results from what is nominally the same enzyme activity (Zhu & Snodgrass, 2004) ^[35]. Molecular diagnostics targeting a single locus, PCR-RFLP or allele-specific PCR for a known kdr, ace or Rdl mutation, are the fastest and cheapest of the three once a marker exists, but they remain blind to resistance conferred by mechanisms outside their designed scope, exactly the failure mode illustrated by the *Diaphorina citri* and *Tetranychus urticae* cases discussed above. Synergist bioassays, co-applying an insecticide with piperonyl butoxide to implicate cytochrome P450 activity, with S,S,S-tributyl phosphorotrithioate to implicate esterases, or with

diethyl maleate to implicate glutathione S-transferase, remain a useful first step precisely because they test a functional hypothesis about mechanism rather than assuming one, though they stop short of pinpointing the specific gene or mutation responsible (Corbel & N'Guessan, 2013) ^[9].

The practical gap this leaves is a resistance-management programme that still relies on choosing one of these three tools rather than combining them as a matter of routine, and the field evidence reviewed here argues fairly strongly against that practice. A programme built entirely on synergist bioassay would have missed the reduced-penetration component contributing to tobacco budworm resistance; one built entirely on kdr genotyping would have missed the P450-driven component of *Helicoverpa armigera* resistance documented by Alvi *et al.* (2012) ^[2]; and one built entirely on AChE activity assay would have wrongly concluded that *Diaphorina citri* organophosphate resistance had no biochemical basis at all, when the correct conclusion was only that AChE was not the basis (Tiwari *et al.*, 2012) ^[29].

Alternatives to conventional chemical rotation are moving from concept toward field testing more quickly than the older literature anticipated. Nano-formulated botanical and microbial preparations are reported to reduce selection pressure on individual detoxification pathways by delivering active ingredient more consistently and at lower application rates than unencapsulated formulations, an approach demonstrated for silica-nanoparticle-encapsulated eucalyptus oil against *Helicoverpa armigera* populations already carrying kdr splice variants and elevated P450 activity, where laboratory trials recorded mortality improvements in the order of forty-five to sixty percent over the unencapsulated formulation (Bharadava *et al.*, 2026) ^[6]. Sprayable double-stranded RNA constructs targeting essential genes in *Spodoptera frugiperda* and related lepidopteran pests represent a still more direct route around existing resistance mechanisms, since gene silencing does not depend on the insecticide reaching a specific enzyme or receptor target at all, though field persistence of dsRNA under ultraviolet exposure and the durability of any RNAi-specific resistance that might itself evolve under sustained use remain open questions rather than settled advantages (Bharadava *et al.*, 2026) ^[6]. None of these approaches removes the underlying evolutionary pressure driving resistance, and the caution these reviews attach to describing them as low-resistance-risk options rather than resistance-proof ones seems the appropriate one to carry forward.

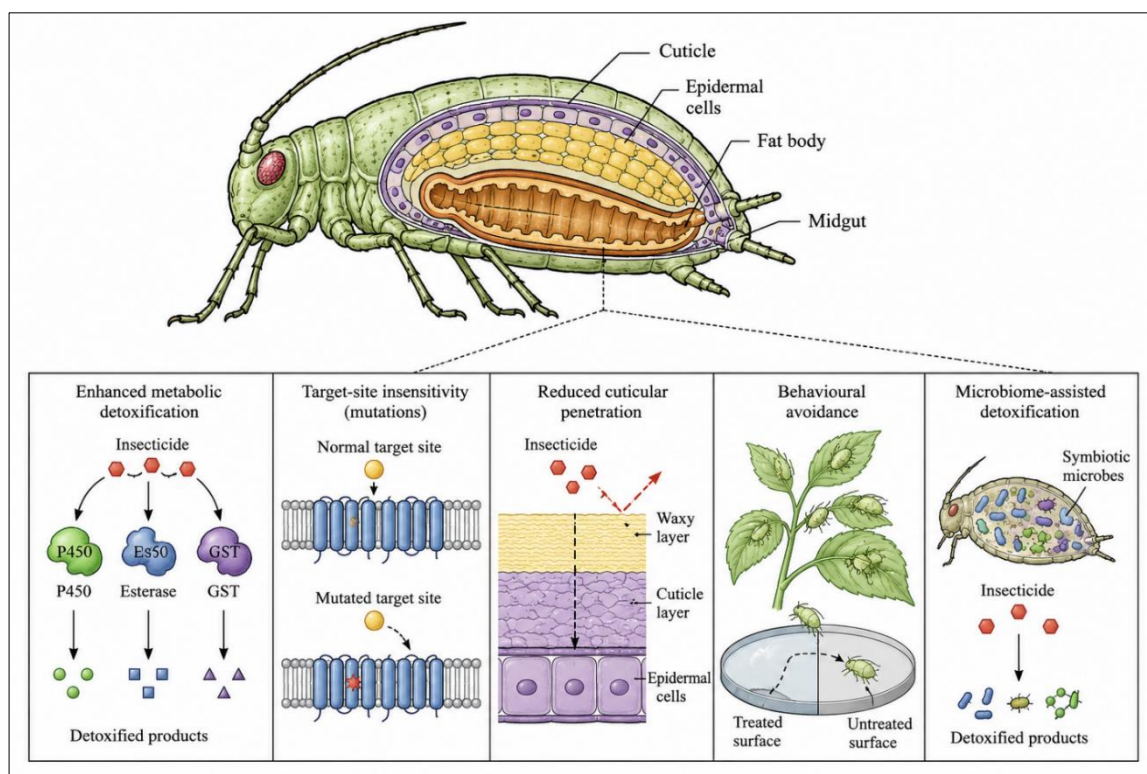
Table1: Major biochemical and physiological resistance mechanisms documented in agricultural insect pests

Mechanism	Molecular basis	Insecticide classes affected	Representative pests	References
Esterase-mediated sequestration/hydrolysis	Gene amplification at E4/FE4 loci increasing hydrolytic capacity	Organophosphates, carbamates, pyrethroids	<i>Myzus persicae</i>	Khan <i>et al.</i> , 2020 ^[18]
Cytochrome P450 over-expression	Cis-regulatory or transcription-factor driven up-regulation	Pyrethroids, neonicotinoids	<i>Myzus persicae</i> ; <i>Helicoverpa armigera</i>	Khan <i>et al.</i> , 2020; Alvi <i>et al.</i> , 2012 ^[18, 2]
Glutathione S-transferase elevation	Increased conjugation of reduced glutathione to electrophilic metabolites	Organochlorines, organophosphates	<i>Musca domestica</i>	Khan <i>et al.</i> , 2020 ^[18]
Acetylcholinesterase modification	Point mutation reducing organophosphate/carbamate binding affinity	Organophosphates, carbamates	<i>Plutella xylostella</i> ; <i>Musca domestica</i>	Khan <i>et al.</i> , 2020 ^[18]
Voltage-gated sodium channel kdr mutation	L1014F substitution reducing channel sensitivity	Pyrethroids, DDT	<i>Ceutorhynchus spp.</i>	Daum <i>et al.</i> , 2024 ^[10]
Voltage-gated sodium channel super-kdr	M918T combined with L1014F	Pyrethroids	<i>Lygus pratensis</i>	Zhang <i>et al.</i> , 2024 ^[14]
Voltage-gated sodium channel double mutation	T929I combined with K1774N, functionally confirmed	Pyrethroids	<i>Megalurothrips usitatus</i>	Gao <i>et al.</i> , 2024 ^[14]
Voltage-gated sodium channel	L1014F combined with M918I	Pyrethroids	<i>Aphis glycines</i>	Valmorbida <i>et al.</i> ,

marker set				2022 ^[30]
Nicotinic acetylcholine receptor mutation	Point mutation in the Mpβ1 D-loop region	Neonicotinoids	<i>Myzus persicae</i>	Bass <i>et al.</i> , 2011 ^[5]
GABA receptor (Rdl) modification	A302S substitution altering chloride-channel gating	Cyclodienes, phenylpyrazoles	<i>Tribolium castaneum</i>	Khan <i>et al.</i> , 2020 ^[18]
Reduced cuticular penetration	Increased cuticular lipid, protein content and sclerotisation	Broad spectrum, synergistic with metabolic mechanisms	<i>Heliothis virescens</i> ; <i>Musca domestica</i>	Saha, 2016 ^[22]
Behavioural avoidance	Altered feeding, resting or oviposition reducing contact	Organochlorines, carbamates, pyrethroids	<i>Plutella xylostella</i> ; <i>Leptinotarsa decemlineata</i>	Simon, 2014; Thenmozhi & Chandrakar, 2026 ^[26, 28]
Microbiome-mediated detoxification	Symbiont-assisted metabolism (Sphingomonas, Wolbachia)	Neonicotinoids	<i>Aphis gossypii</i> ; <i>Nilaparvata lugens</i>	Thenmozhi & Chandrakar, 2026 ^[28]
Reduced midgut toxin binding	Reduced receptor binding of Cry proteins	Bacillus thuringiensis toxins	<i>Helicoverpa armigera</i>	Alvi <i>et al.</i> , 2012 ^[2]

Table-2: Quantitative resistance-ratio and target-site mutation frequency data reported for major agricultural pests

Pest species	Insecticide	Reported resistance ratio or mutation frequency	Reference
<i>Bemisia tabaci</i>	Imidacloprid	58 to 126 fold (Guatemalan B-biotype)	Byrne <i>et al.</i> , 2003 ^[7]
<i>Bemisia tabaci</i>	Imidacloprid	3.7 to 26.3 fold (Florida, 2000 to 2007)	Schuster <i>et al.</i> , 2010 ^[23]
<i>Bemisia tabaci</i>	Imidacloprid	86 fold (laboratory selection, 5 generations)	Khalid <i>et al.</i> , 2021 ^[17]
<i>Plutella xylostella</i>	Chlorantraniliprole	684.5 fold (laboratory-selected strain)	Qin <i>et al.</i> , 2018 ^[19]
<i>Myzus persicae</i>	Imidacloprid	106.9 fold (field population, China)	Hu <i>et al.</i> , 2023
<i>Myzus persicae</i>	Beta-cypermethrin	324 fold (field population, China)	Hu <i>et al.</i> , 2023 ^[16]
<i>Tetranychus urticae</i>	Abamectin	2,226 to 21,141 fold (RR50)	Díaz-Arias <i>et al.</i> , 2019 ^[11]
<i>Helicoverpa armigera</i>	Cypermethrin	1,950 fold (field population, Pakistan)	Alvi <i>et al.</i> , 2012 ^[2]
<i>Leptinotarsa decemlineata</i>	Imidacloprid	10.1 to 18.2 fold (2013); 1.8 to 11.2 fold (2014)	Clements <i>et al.</i> , 2016 ^[8]
<i>Musca domestica</i>	Diazinon	62.5 to 309.8 fold (field population, Riyadh)	Abobakr <i>et al.</i> , 2022 ^[1]
<i>Ceutorhynchus</i> spp.	Pyrethroids (kdr L1014F)	0 to 100 percent homozygote frequency across populations	Daum <i>et al.</i> , 2024 ^[10]
<i>Lygus pratensis</i>	Lambda-cyhalothrin (kdr/super-kdr)	Up to 60 percent combined homozygous/heterozygous frequency	Zhang <i>et al.</i> , 2024 ^[14]
<i>Aphis glycines</i>	Pyrethroids (kdr L1014F + M918I)	Field-evolved, marker-confirmed in resistant phenotypes	Valmorbida <i>et al.</i> , 2022 ^[30]
<i>Megalurothrips usitatus</i>	Pyrethroids (T929I + K1774N)	Functionally confirmed in field-resistant Hainan strains	Gao <i>et al.</i> , 2024 ^[14]

**Fig 1:** Proposed convergence of metabolic detoxification and target-site insensitivity pathways in a field-resistant agricultural pest population, integrating enzyme-activity and genotyping evidence reviewed for *Myzus persicae*, *Helicoverpa armigera* and *Bemisia tabaci*.

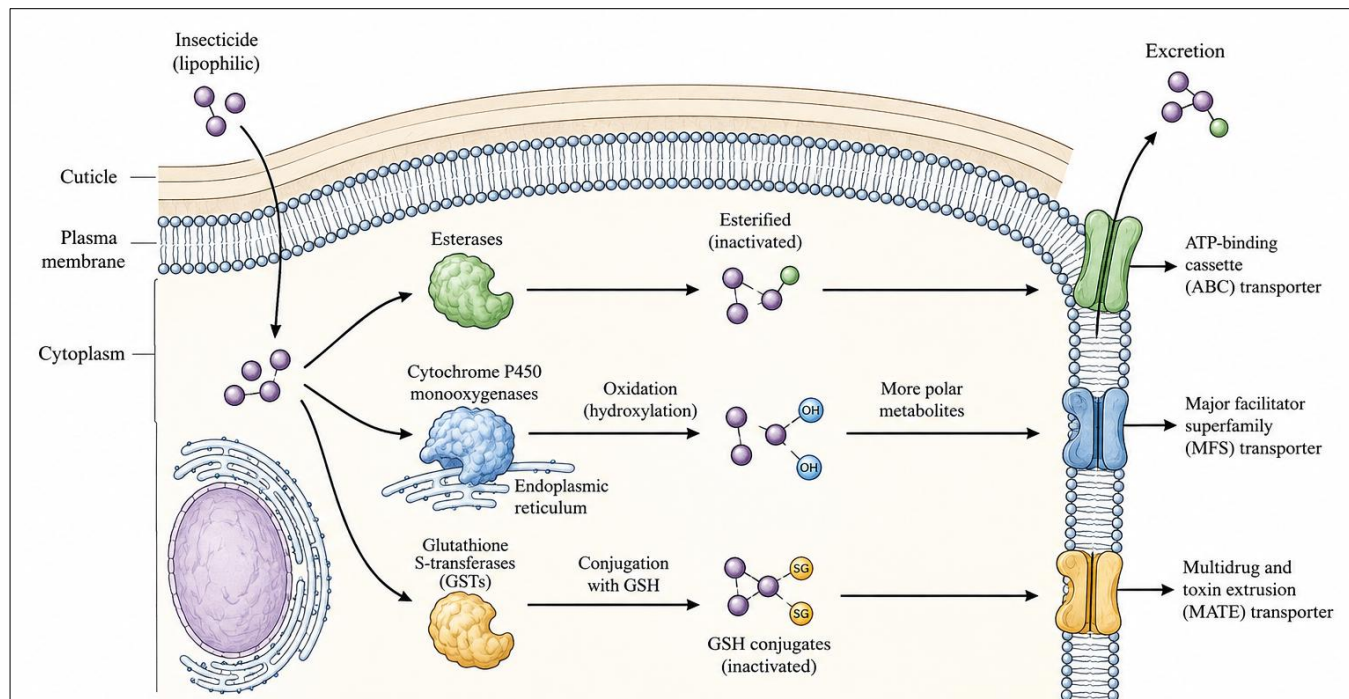


Fig 2: Schematic trajectory of imidacloprid resistance ratio (RR50) in Florida field populations of *Bemisia tabaci* biotype B across a multi-year monitoring period, illustrating non-monotonic fluctuation and reversion under relaxed selection pressure, redrawn from data reported by Schuster *et al.* (2010) [23].

7. Conclusion

Taken as a whole, the picture that emerges from this body of work is one of layered, population-specific resistance rather than a fixed catalogue of mechanisms waiting to be matched against a given pest species. Metabolic detoxification and target-site insensitivity are not competing explanations so much as concurrent processes that, in the majority of field-resistant populations examined here, operate together and reinforce one another, with reduced cuticular penetration and, increasingly, symbiont-assisted metabolism acting as quieter contributors that amplify whichever primary mechanism a population has already acquired. Reported resistance ratios and enzyme-activity fold-changes carry less inherent stability than the format of a single published study tends to suggest, since the choice of assay substrate, reference strain and sampling season each shift the number independently of any underlying change in the insect. That variability is not a weakness of the field so much as a warning against treating any single number as a settled fact about a pest population.

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