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Gaining insights into epigenetic memories through artificial intelligence and omics science in plants[oo]

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ABSTRACT

Plants exhibit remarkable abilities to learn, communicate, memorize, and develop stimulus-dependent decision-making circuits. Unlike animals, plant memory is uniquely rooted in cellular, molecular, and biochemical networks, lacking specialized organs for these functions. Consequently, plants can effectively learn and respond to diverse challenges, becoming used to recurring signals. Artificial intelligence (AI) and machine learning (ML) represent the new frontiers of biological sciences, offering the potential to predict crop behavior under environmental stresses associated with climate change. Epigenetic mechanisms, serving as the foundational blueprints of plant memory, are crucial in regulating plant adaptation to environmental stimuli. They achieve this adaptation by modulating chromatin structure and accessibility, which contribute to gene expression regulation and allow plants to adapt dynamically to changing environmental conditions. In this review, we describe novel methods and approaches in AI and ML to elucidate how plant memory occurs in response to environmental stimuli and priming mechanisms. Furthermore, we explore innovative strategies exploiting transgenerational memory for plant breeding to develop crops resilient to multiple stresses. In this context, AI and ML can aid in integrating and analyzing epigenetic data of plant stress responses to optimize the training of the parental plants.

Keywords: deep learning, DNA methylation, gene expression, machine learning, stress memory, transgenerational inheritance

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INTRODUCTION—GAINING INSIGHTS INTO EPIGENETIC MEMORIES IN PLANTS

The remarkable ability of plants to adapt to highly contrasting and challenging environments is a key aspect of their biology. This is crucial for sessile organisms, which cannot escape threatening environmental constraints. In particular, they have acquired the ability to store information from previous experiences and subsequently use or erase it (Gallusci et al., 2023; Hemenway and Gehring, 2023). As a result of this adaptability, the idea of plant memory has emerged, along with the concept that plants have evolved a specific kind of intelligence (van Loon, 2016; Calvo et al., 2020). Indeed, these remarkable plant capacities do not depend on cognitive abilities but are entirely mediated by cellular processes. These extend from the storage of specific metabolites (Schwachtje et al., 2019), signaling molecules (Sadhukhan et al., 2022), messenger RNAs (mRNAs), post-translational protein modification, and RNA polymerase stalling (Crisp et al., 2016), to the stable and heritable remodeling of chromatin domains, a process known as epigenetics (Lämke and Bäurle, 2017; Guarino et al., 2022). While all these biochemical and molecular processes contribute to plant memory, they act on different time scales, from minutes to months and even years, but also at various levels, from individual cells to entire organisms and even at populations, leading to an environmental memory (Auge et al., 2023). Short-term memory mechanisms are more related to the rapid plant acclimation to stresses, a process termed priming or hardening and may involve all the aforementioned cellular processes (Hilker and Schmülling, 2019; Liu et al., 2022). However, while metabolic processes are generally considered important for the short-term memory of stresses, transcriptional memory mechanisms, such as RNA polymerase II stalling or mRNA stability, and those involving epigenetic regulations, may act over longer durations (see below; Pastor et al., 2013). Consequently, the latter are major contributors to the long-term memory of plant cells. They form the basis of cellular memory and enable cells to retain past experiences, thereby determining the organism's memory through a process called somatic memory, which describes the transmission of information via mitosis. Somatic memory mediated by epigenetic mechanisms is particularly crucial for information storage in the meristem and has been described in the case of the vernalization process in *Arabidopsis thaliana* (Baulcombe and Dean, 2014). How the cell population of meristem evolves over time and leads to a change in the epigenetic state of the meristem that will allow flowering months later has been modeled, showing the progressive evolution of meristem cell epigenetic state as a function of cold and the change in meristem state (Song et al., 2012). Of course, this memory is reset during sexual reproduction, requiring all processes to restart in the offspring. In the context of climate change, the plant somatic memory is central to plant acclimation, as it allows plants to "remember" past exposure to stresses and contribute to a more efficient response to subsequent events, thereby enhancing their resilience. In addition, there is increasing evidence for the transmission of epigenetic information during sexual reproduction (Quadrana and Colot, 2016). In most reported cases, such memories were reported when new epigenetic information was established during periods of stress in parental plants, maintained in meristems before transmission to gametes, and after fertilization in the newly formed embryo (Anastasiadi et al., 2021). While intergenerational epigenetic inheritance has been demonstrated (Wibowo et al., 2016), clear evidence for transgenerational epigenetic memories in the absence of new stress application to the progeny remains limited (Quadrana and Colot, 2016; Van Dooren et al., 2020). Interestingly, intergenerational memory appears more efficient in clonally propagated plants, as demonstrated with heat stress in wild strawberries (López et al., 2024) and drought stress in poplar (Vanden Broeck et al., 2018), clover (Rendina González et al., 2018), or overgrazing (Yin et al., 2023). Furthermore, perennials can also develop a trans-annual memory that may be stored in the apical meristem during winter (Le Gac et al., 2018), although this process may vary between plant species, stress intensity, and the period of stress application. Ultimately, the diversity of these memory mechanisms relies on several different molecular mechanisms and allows plants to adapt their behavior when facing environmental challenges and optimize the trade-off between growth, yield and survival at the individual and population levels. These findings are highly relevant not only for wild populations but also in the context of agriculture, as harnessing plant memories, including those based on epigenetic mechanisms, may represent a promising new tool for developing crops that are better adapted to environmental challenges, as discussed in several recent reviews (Gallusci et al., 2017, 2023; Berger et al., 2023; Ganie et al., 2024; Miryeganeh, 2025). However, addressing the critical knowledge gaps regarding the molecular mechanisms underlying stress memory is now required to develop innovative strategies to enhance crop resilience to environmental challenges and thereby support food security in the context of climate change.

EPIGENETIC REGULATION OF PLANT DEFENSE RESPONSES AGAINST ENVIRONMENTAL STRESSES

Facing continuous biotic and abiotic challenges that affect their growth, development, productivity, and environmental adaptability, plants have evolved sophisticated defense strategies. Unlike animals, which rely on specialized or adaptive immunity, plants utilize innate immunity to combat biotic stresses (Bentham et al., 2020). Their multilayered defense mechanisms involve epigenetic regulation through DNA methylation, histone modifications, chromatin remodeling and

non-coding RNAs (ncRNAs), comprising short (e.g., microRNAs (miRNAs), small interfering RNAs (siRNAs)) and long non-coding (lncRNAs) types (Figure 1). These epigenetic mechanisms are crucial for shaping both dynamic and heritable responses to stress.

DNA methylation and demethylation

DNA methylation in plants involves the addition of a methyl group to the 5-position of cytosine residues, primarily in CG, CHG, and CHH contexts. This process contributes to the silencing of transposable elements (TEs), maintaining genome stability and modulating gene expression (Li et al., 2022a; Mishra et al., 2024). In response to environmental stimuli, plants reprogram their methylation patterns to activate or repress specific genes by modulating access to the transcriptional machinery. Lower DNA methylation levels in specific genomic regions have been linked to increased disease resistance in plants, mainly via the activation of

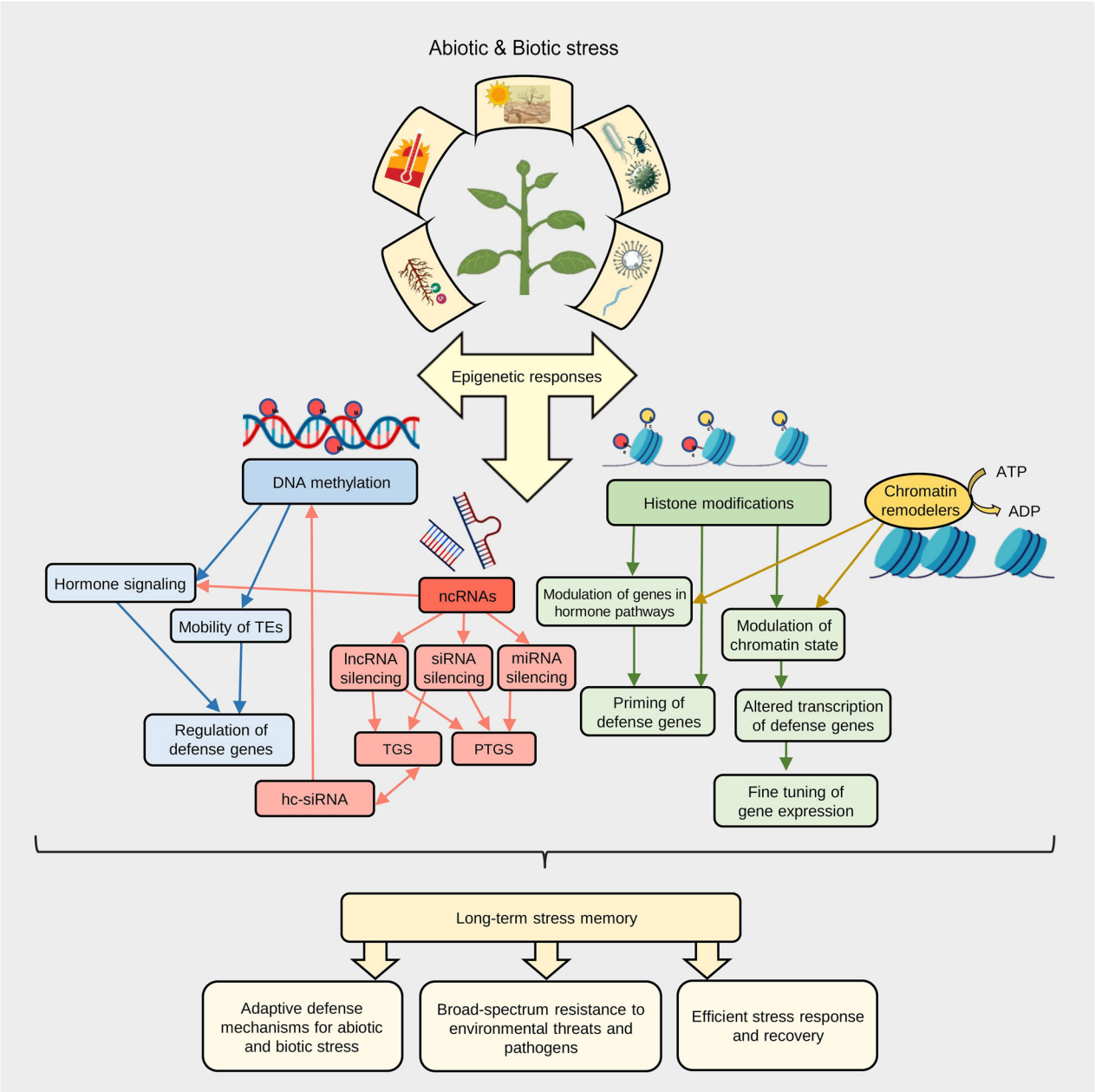

Figure 1. Schematic overview of epigenetic mechanisms in plant responses to biotic and abiotic stresses

The diagram highlights the involvement of DNA methylation, histone modifications, chromatin remodeling, and non-coding RNAs (ncRNAs; including lncRNAs, siRNAs, and miRNAs) in the regulation of defense genes and hormonal signaling pathways. These coordinated processes are crucial for establishing long-term stress memory, facilitating adaptive responses, and enhancing plant resilience against environmental challenges. hc-siRNAs, heterochromatic small interfering RNAs; miRNAs, microRNAs; ncRNAs, non-coding RNAs; lncRNAs, long non-coding RNAs; siRNAs, small interfering RNAs; TEs, transposable elements; TGS, transcriptional gene silencing; PTGS, post-transcriptional gene silencing.

salicylic acid (SA)-dependent defense pathways, although this response varies depending on the type of stress, tissue and developmental stage. Active DNA demethylation, mediated by DNA glycosylases such as DEMETER (DME)-like proteins, Repressor of Silencing 1 (ROS1), and related enzymes, is equally important in plant stress responses. These enzymes remove 5-methylcytosine (m^5C) marks from DNA, creating an apurinic/apyrimidinic (AP) site which is subsequently repaired by the addition of non-methylated cytosines, enabling the reactivation of stress- and defense-related genes (Schumann et al., 2019; Halter et al., 2021; Farkas and Dobránszki, 2024). The dynamic balance between methylation and demethylation allows plants to flexibly regulate gene expression during immediate stress responses. Furthermore, pathways like RNA-directed DNA methylation (RdDM) may contribute to the establishment of longer-term epigenetic memory under recurring environmental stress conditions.

Histone modifications and chromatin dynamics

Histone proteins undergo 100s of post-translational modifications, including acetylation, methylation and ubiquitination, which significantly influence chromatin organization and accessibility (Mierziak and Wojtasik, 2024). These modifications can either promote or repress transcription, depending on their specific type and location (Figure 1). Histone acetylation, typically associated with transcriptional activation, is catalyzed by histone acetyltransferases (HATs), which add acetyl groups to lysine residues. This neutralizes their positive charge, loosens chromatin structure and facilitates access for transcription factors and RNA polymerase to genes, including stress-responsive genes. Conversely, histone deacetylases (HDACs) remove acetyl groups, leading to chromatin condensation and transcriptional repression (Ramirez-Prado et al., 2018). For instance, in rice, the HDAC HDA704 is recruited by the transcription factor OsWR2 to deacetylate H4K8 in the promoter of *OsABI5* under drought conditions, thereby repressing its expression and contributing to drought stress tolerance (Guo et al., 2023a). Histone methylation on lysine and arginine residues can either activate or repress genes, depending on the specific residue modified and the degree of methylation state (mono-, di-, or tri-methylation), allowing plants to finely adjust gene activity in response to stress cues (Jaskiewicz et al., 2011). Histone ubiquitination, particularly monoubiquitination of histone H2B, is generally linked to transcriptional activation and contributes to plant immunity and tolerance to abiotic stresses (Zhang et al., 2015; Ma et al., 2019; Chen et al., 2020). Through precise coordination of histone modifications, plants activate complex defense mechanisms tailored to specific stressors, while simultaneously balancing responses to avoid metabolically costly overreaction that could compromise cellular homeostasis and growth.

Chromatin remodeling and nucleosome dynamics

Histone modifications act as chemical tags on chromatin signaling transcriptional accessibility, while adenosine triphosphate (ATP)-dependent chromatin remodelers physically reposition or evict nucleosomes to either permit or restrict access to specific DNA regions by the transcriptional machinery. These ATP-dependent remodeling complexes alter chromatin architecture and gene expression patterns using energy from ATP hydrolysis (Huang and Jin, 2022). In plants, key members of the SNF2 family (a family of helicase-like proteins) BRAHMA (BRM), SPLAYED (SYD), and DECREASE IN DNA METHYLATION 1 (DDM1) play a major role in the regulation of gene expression, particularly in defense responses (Bhadouriya et al., 2021). BRAHMA and SYD are directly involved in transcriptional regulation of stress-responsive genes, whereas DDM1 facilitates the access of DNA methyltransferases to heterochromatic regions, thereby indirectly influencing the expression of defense-related genes through epigenetic silencing mechanisms. Chromatin remodelers modulate transcription by shifting or evicting nucleosomes, especially at loci involved in stress signaling, hormone response and pathogen defense. As illustrated in Figure 1, their activity is tightly coordinated with DNA methylation and histone modifications to provide precise control of gene expression. This remodeling is particularly important under stress, allowing for the rapid activation of silenced genes without permanent genomic alterations, while also supporting stable epigenetic memory when necessary.

RNA-mediated silencing and systemic signaling

Small RNAs (sRNAs) are short, ncRNA molecules that regulate gene activity at both transcriptional gene silencing (TGS) and post-transcriptional gene silencing (PTGS) levels (Zhan and Meyers, 2023). An important defense mechanism in plants is gene silencing, mediated by specific types of sRNAs—miRNAs and siRNAs, which target plant mRNAs, and viral and subviral RNAs for sequence-specific degradation and modulation of transcriptional reprogramming (Iqbal et al., 2021). While miRNAs primarily induce PTGS, they can occasionally function in TGS (Basso et al., 2019). Depending on their length, siRNAs can silence genes by targeting mRNAs at the PTGS level or by affecting specific genomic loci at the TGS level through epigenetic changes (Figure 1) (Basso et al., 2025). Small RNAs also modulate plant hormonal pathways and enhance plant resistance by suppressing specific negative regulators (Cambiagno et al., 2018; Waheed et al., 2021). Mutations affecting sRNA biogenesis or the RdDM pathway may increase plant susceptibility to stress (Cai et al., 2018; Basso et al., 2025). In the RdDM pathway, heterochromatic siRNAs (hc-siRNAs) guide *de novo* DNA methylation, which activates defense-related genes, including nucleotide-binding leucine-rich repeat receptors (NLRs) and other genes encoding signaling proteins, thereby triggering tolerance responses and balancing growth and defense (Papareddy et al., 2020). Endogenous sRNAs not only act within the cell of origin but can also move through plasmodesmata and the vascular system to systematically trigger gene silencing (Molnar et al., 2011). In turn, exogenous sRNAs have a similar effect on plants and interacting organisms through environmental or cross-kingdom RNA interference (RNAi) (Cai et al., 2018).

In addition to sRNAs, lncRNAs also contribute to gene regulation under stress. They can act as precursors for siRNAs, decoys for miRNAs or by directly guiding chromatin-modifying complexes to specific loci, thereby influencing TGS (Chekanova, 2015). Some lncRNAs participate in the RdDM pathway, functioning as scaffold RNAs or recruiting RNA polymerase V complexes to direct methylation of TEs or stress-related genes (Böhmdorfer et al., 2016). The exchange of sRNAs mediates interactions between host plants and pathogens, as seen in cotton plants infected by *Verticillium dahlia*. The host plant produces miR166 and miR159 which are exported to the *V. dahlia* hyphae, to silence two genes required for disease (Zhang et al., 2016). Conversely, pathogens like *Botrytis cinerea* can deliver sRNAs into cells of *A. thaliana* and tomato (*Solanum lycopersicum* L.), where they load onto the plant RNA-induced silencing complex (RISC) to suppress plant immunity (Weiberg et al., 2013). The ability to control the growth of fungi, such as those that cause powdery mildew and rust, by sRNA uptake is being utilized to control these pathogens. Host-induced gene silencing (HIGS) results in the silencing of a pathogen-specific gene through the *in planta* expression of double-stranded RNA (dsRNA) homologous to the pathogen target gene of interest (Kim and Rossi, 2008; Basso et al., 2025). Several genes related to transcription, host colonization, respiration, glycosylation, chitin synthesis, and virulence have been targeted for RNAi-mediated silencing (Sharma et al., 2019; Saito et al., 2022). Betti et al. (2021) showed that plant cells can take up exogenous naked miRNAs secreted by other plants or artificially synthesized and delivered. Therefore, this acts as a means of communication between neighboring plants, and once inside, it can generate a non-cell-autonomous silencing signal (Voinnet, 2005). Exogenous miRNAs have also been shown to alter plant phenotype (Betti et al., 2021). Heterografting experiments have shown transgene movement from potato rootstock to suppress specific genes in tobacco scion (Kasai et al., 2016) and between grapevine and sweet cherry trees (Zhao et al., 2020a). Collectively, these findings highlight the remarkable ability of both exogenous and endogenous sRNAs to move through continuous vascular connections and induce changes.

In summary, epigenetic regulation is essential for plant stress response, enhancing resistance to various environmental disturbances (Figure 1). DNA methylation, histone modifications, chromatin remodeling, and ncRNAs not only enable adaptive responses and contribute to heritable stress memories but also offer promising strategies for advancing environmentally friendly agricultural practices to improve food security in a stress-rich world.

EPIGENETIC MECHANISMS UNDERLYING PLANT PRIMING

Priming in plants can be induced by applying mild stress or using signal molecules as elicitors. Signaling with various compounds, including volatile organic compounds (VOCs), or nucleic acids like sRNAs and DNA, is a natural phenomenon in plants (Ali et al., 2013; Duran-Flores and Heil, 2018; Marzec, 2022; Onosatu et al., 2022; Ruf, 2022; Dobránszki et al., 2025). Primed plants display enhanced fitness and a greater capacity to respond more effectively to environmental stimuli (Hilker and Schmülling, 2019). This enhanced responsiveness is mediated through diverse mechanisms, including epigenetic processes that contribute to stress memory (Turgut-Kara et al., 2020). Harris et al. (2023) aptly termed these mechanisms "blueprints" that confer resistance or tolerance to recurrent stress. Our current understanding of plant stress memory, priming and the primed state largely emerged from omics investigations, such as epigenomics, transcriptomics, proteomics, and metabolomics and their correlation with phenotypic characterization. As previously mentioned, the duration of a stress memory is determined by the longevity of the epigenetic changes underlying the primed state. Somatic memory may be either short-term, lasting up to 7–10 d (Jaskiewicz et al., 2011; Po-Wen et al., 2013; Schillheim et al., 2018; Pardal et al., 2021; Sheikh et al., 2023), or long-term, persisting through two or more phenological phases (Wilkinson et al., 2023). Priming can target both nearby and distant Type-I and Type-II memory genes (Harris et al., 2023).

Histone marks of short-term stress memory

Memory storage of abiotic stresses (such as drought, hyperosmotics, salinity, heat, cold, light, and trace metal stresses, etc.) lasting 3–14 d has been primarily associated with H3 and H4 histones in various plant species. This typically involves methylation and acetylation of H3 (H3K4me2/3, H3K27me2/me3, H3K9ac, and H3K9me3) and H4 (H4R3sme2, H4ac, and H4K5/8/12/16ac). Notably, H3 phosphorylation (H3T3ph) was also observed in *A. thaliana* during tolerance to osmotic stress. Additionally, H2 monoubiquitination has been associated with drought and salt tolerance in rice (*Oryza sativa* L.) (Ma et al., 2019; Chen et al., 2020), as well as with drought tolerance in *A. thaliana* and cotton (*Gossypium hirsutum* L.) (Chen et al., 2019a). Low levels of H3 methylation (H3K27me3) have been shown to prime *A. thaliana* for increased thermotolerance under recurrent heat stress by altering the transcription of Type-II memory genes (*HSP22* and *HSP17.6C*) (Yamaguchi et al., 2021).

Plant memory of pathogen infection was mainly stored in H3 and H4 core histone proteins by methylation (H3K4me3 and H3K4me2) and/or acetylation (H3K9ac, H4K12ac, and H3K9K14ac) (Jaskiewicz et al., 2011). Priming of *A. thaliana* with sulforaphane (1-isothiocyanato-4-methylsulfinylbutane), a secondary metabolite in some crucifers (Schillheim et al., 2018), induced H3 (H3K4me3 and H3K9ac) trimethylation and acetylation at the promoter and the proximal region of the *WRKY6* and *PDF1.2* genes. The latter serves as a marker gene for the activation of the jasmonate signaling pathway after infection (Koornneef and Pieterse, 2008). However, H3 modification was not detected in the *PR1* defense gene, a marker gene of the SA signaling pathway during infection with *Pectobacterium carotovorum* (Penninckx et al., 1996;

Koornneef and Pieterse, 2008; Schillheim et al., 2018). In contrast, when priming was induced by β-aminobutyric acid (BABA), methylation (H3K4me2) and acetylation (H3K9K14ac) of H3, and priming of *PR1* (gene encoding pathogenesis-related protein 1) occurred, but *PDF1.2* (gene encoding plant defensin 1.2) was not primed upon infection with the same pathogen (Po-Wen et al., 2013) (Figure 2).

Furthermore, Sheikh et al. (2023) showed that the linker histone, H1, also plays a role in the regulation of histone acetylation (H3K56ac) and methylation (H3K4me3 and H3K27me3), as well as DNA methylation of defense-related genes in *A. thaliana* during priming by flagellin 22 (flg22) peptides (Figure 2).

Changes in DNA methylation during short-term stress memory

DNA methylation change at cytosine sites (m^5C) have been observed during hyperosmotic and drought stresses (Guarino et al., 2022; Harris et al., 2023), while methylation at adenine sites (m^6A) was noted during salinity priming (Zhang et al., 2018). Modifications in m^5C-type DNA methylation in response to drought stress may be different, such as hyper- or hypomethylation, depending on the susceptibility or earlier adaptation state of a plant variety. Hypermethylation was detected in non-adapted or susceptible varieties, whereas hypomethylation was found in previously adapted or tolerant varieties of rice and white clover (*Trifolium repens* L.) (Gayacharan and Joel, 2013; Rendina González et al., 2018). Similarly, salinity stress priming resulted in either increased or decreased m^5C methylation depending on the plant species (Guarino et al., 2022).

DNA hypomethylation (m^5C) also plays a significant role in the formation of somatic memory and, consequently, in defense priming (Figure 2). Epigenetic changes in pathogen receptor genes neighboring TEs (i.e., genes for pattern recognition receptors (*PRR*s) and nucleotide-binding repeats (*NLR*s)) may contribute to this memory. DNA hypomethylation in response to infection of *A. thaliana* with *Pseudomonas syringae* pv. *tomato* upregulated TE expression, leading to the induction of *NLR*s. Furthermore, sRNAs appear to participate in the silencing activated TEs, thus controlling the expression of both TEs and pathogen receptor genes (Cambiagno et al., 2018). Specifically, DNA hypomethylation, in the CHH context of stress-responsive genes or their regulatory genes was the main feature of enhanced resistance to *P. syringae* pv. *tomato* in tomatoes primed with BABA (Catoni et al., 2022).

Chromatin remodeling and nucleosome repositioning during short-term stress memory

Histone modifications (e.g., acetylation, methylation, ubiquitination and phosphorylation) influence chromatin structure

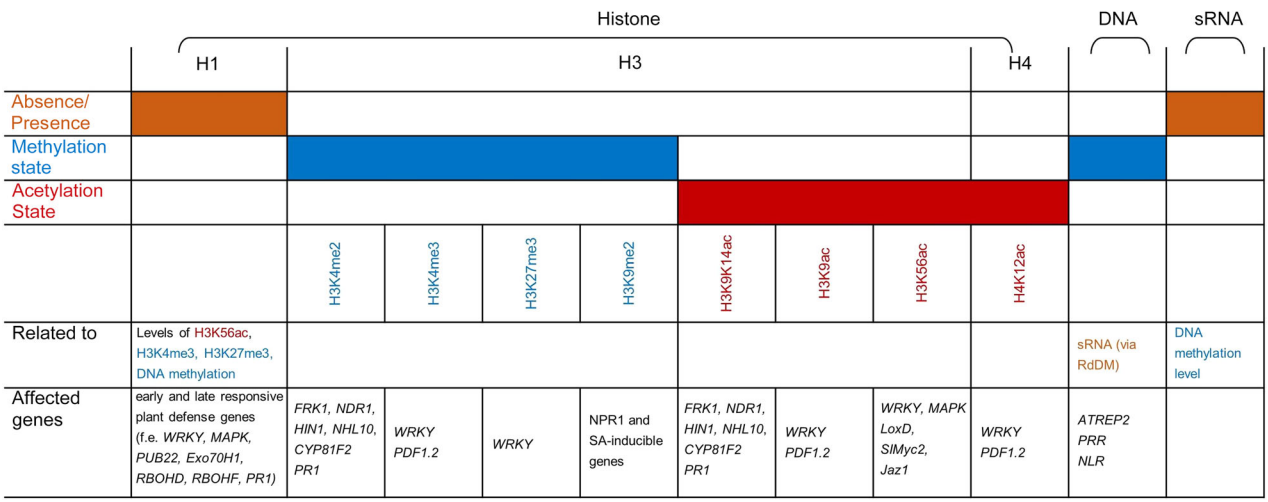

Figure 2. Epigenetic background of priming for enhanced resilience to biotic stresses

This figure illustrates the main types of epigenetic modifications identified during priming and their relationship to each other in preparing plants for more effective defense responses against pathogens. Examples of affected defense-related genes and the corresponding epigenetic marks are provided. Key examples include the following. (i) Priming of *Arabidopsis thaliana* against *Pseudomonas syringiae* pv. *maculicola* involved H3 modifications on the promoters of defense genes (WRKY6, WRKY9, and WRKY53), like H3K4 trimethylation at Lys 4 (H3K4me3) in npr1, sni1, and cpr1 mutants and thereby their enhanced readiness. In addition, acetylation of H3 and H4 (H3K9ac and H4K12ac) histones was also increased at the promoters of some WRKYs due to priming (Jaskiewicz et al., 2011). (ii) Sulforaphane priming in *A. thaliana* reduced the plant susceptibility to downy mildew (*Hyaloperonospora arabidopsidis*). In response to H3 modifications (H3K4me3 and H3K9ac), chromatin unpacking was detected associated with WRKY6 and PDF1.2 transcription sites (Schillheim et al., 2018). (iii) β-aminobutyric acid (BABA) treatment primed pattern-triggered immuniity (PTI)-responsive genes (FRK1, NDR1, HIN1, NHL10, and CYP81F2) in *A. thaliana*, leading to enhanced expression upon infection with *Pectobacterium carotovorum* ssp. *carotovorum* or treatment with its epitopes (flg22, elf26 (EF-Tu)). This primed state of PTI-related genes was associated with enrichment of H3 acetylation (H3K9K14ac) and methylation (H3K4me2 resulting in open chromatin at their promoter regions. (iv) Histone H1 can influence H3 modifications (H3K56ac, H3K4 me3, and H3K27me3) as well as DNA methylation of defense-related genes (Sheikh et al., 2023). (v) DNA hypomethylation can increase the expression of transposable elements (TEs) located near pathogen receptor genes (e.g., pattern recognition receptors (PRRs) and nucleotide-binding repeats (NLRs)), while sRNAs participate in silencing these TEs via RNA-directed DNA methylation (RdDM) (Cambiagno et al., 2018). SA, salicylic acid; sRNA, small RNA.

and, consequently, gene expression. During stress, to facilitate gene expression from tightly packaged DNA regions, particularly those containing stress-related genes, the DNA must become accessible to protein factors or complexes. Post-translational modifications of chromatin remodeling complexes and histone proteins modulate nucleosome assembly and spacing, thereby regulating the DNA accessibility (Yung et al., 2021).

Heat stress priming in *A. thaliana* requires increased activity of FORGETTER1 (FGT1), which interacts with chromatin remodelers from the SWI/SNF and ISWI-families. This interaction affects nucleosome dynamics and thereby modulates nucleosome occupancy at Type-I memory genes, such as *HSA32* (Brzezinka et al., 2016).

Nucleosome repositioning and chromatin opening (e.g., changes in chromatin accessibility) during priming to biotic stress are also associated with changes in transcription. Altered nucleosome positioning has been observed in response to flg22 treatment in more than half of the flg22-regulated genes in *A. thaliana* and *Nicotiana benthamiana* Domin (Pardal et al., 2021). The identification of these altered nucleosome patterns in non-differentially expressed genes (DEGs) (both within gene bodies and their promoters) suggests that these genes were primed for changes in gene expression.

Epigenetic marks of long-term somatic stress memory

Long-term somatic memory, lasting for 3 weeks, was established for herbivore attack in *A. thaliana* plants previously primed with jasmonate. In response to jasmonate treatment, DNA hypomethylation of *ATREP2* TEs occurred. Hypomethylated *ATREP2* then produced 21-nt siRNAs that bind to ARGONAUTE1 within RISC. The siRNAs, enriched with sequences from immunity-related genes, are proposed to mediate trans-regulation and contribute to the long-term memory of jasmonate-dependent immunity (Wilkinson et al., 2023). Luna et al. (2014) detected 28-d-long priming in *A. thaliana* triggered by BABA. This long-term priming was related to H3K9m2 and DNA methylation (in the CHG context) mediated by KYP histone methyltransferase. It affected SA-inducible genes and *NPR1* by silencing their suppressor genes.

TRANSGENERATIONAL MEMORIES AND CROP BREEDING

Although priming is usually transient, fading within a week or a few weeks and certainly within an individual's lifetime, several studies demonstrated inter- or transgenerational inheritance of priming (Lämke and Bäurle, 2017; Guarino et al., 2022; Harris et al., 2023). From an acclimation and adaptation perspective maintaining a primed state is beneficial for plants if it confers a survival and adaptation advantage by preserving the memory of environmental stress (Lämke and Bäurle, 2017). Naturally occurring or induced epigenetic variations can be utilized to alter phenotypic diversity, thereby achieving stress resistance. These variations can be employed to develop stress-resilient crops and, if heritable, to breed plants with enhanced resilience. As this method relies on changes in gene function without altering the gene sequence, it offers the advantage of preserving innate genetic diversity (Sampson et al., 2024).

Intragenerational memory-based priming can be applied in plant breeding to enhance adaptation and, consequently, improve resilience to a stressor within a growing season. Exploring opportunities in cross-stress priming can lead to the development of crops that are resilient to cross-stress or even multiple stresses. In cross-stress priming, the initial stress, whether biotic or abiotic, differs from the subsequent stress(es) but allows for increased plant tolerance to the latter stress(es) due to the synergistic defense signaling pathway against stresses (Liu et al., 2022). For instance, repeated application of abiotic stress (salt, drought, or cold) in *A. thaliana* showed increased resistance against *P. syringae* pv. *tomato*. This cross-priming was associated with H3 modifications (H3K3me2/me3 and H3K9K14ac) in pattern-triggered immunity-related genes, such as *WRKY53*, *FRK1*, and *NHL10* (Singh et al., 2014).

The transfer of priming to offspring may lead to increased stress resilience against abiotic or biotic stress, and even resilience to cross- or multiple stresses, in the next generation(s) (Liu et al., 2022). Flg22 treatment induced epigenetic changes in *A. thaliana* that led to a higher frequency of somatic homologous recombination, which persisted for at least four generations, indicating the epigenome's adaptive flexibility to environmental effects (Molinier et al., 2006). Next-generation and transgenerational acquired resistance to pathogens in *A. thaliana* and potato plants was linked to epigenetic marks of H3K9ac, H3K9me2/3, H3K4me2, H3K27me3, and DNA hypomethylation affecting transcription of near or far Type-I or Type-II memory genes (Sánchez et al., 2016; Meller et al., 2018; Furci et al., 2019). Four epiQTLs were identified in epigenetic recombinant inbred lines (epiRILs) of *A. thaliana* resistant to *Hyaloperonospora arabidopsis*. Priming and defense response were associated with DNA hypomethylation at some pericentric regions in *A. thaliana* (Furci et al., 2019). Transgenerational priming of salt tolerance was related to DNA hypermethylation of Type-I memory genes in *A. thaliana* (Wibowo et al., 2016). Priming for heat tolerance was connected to histone mark (H3K27me3) or TE activation caused by siRNA synthesis in *A. thaliana* (Liu et al., 2019a) while being connected to miR168 in *Brassica rapa* L. (Bilichak et al., 2015).

The transfer mechanism of epigenetic marks to progenies, that is the inheritance of stress memory, depends not only on the type, strength, and exposure period of the stress but also on the plant's reproductive mode (Gallusci et al., 2023). In asexual plant propagation, a stress-primed epigenetic state is transmitted to the next generation through mitosis of the cells from which the next generation develops. Recent studies suggest that the epigenetic inheritance of stress-induced epigenetic state is likely to be sustained, as demonstrated for

poplar (Vanden Broeck et al., 2018) and strawberry (López et al., 2024), although variations may occur depending on the type of asexual propagation. However, for clonally propagated crops, this may provide an innovative approach to train parental plants to improve the tolerance of their progenies to different or eventually multiple stress resilience (Epi-trained plants; Figure 3) (Liu et al., 2022; Berger et al., 2023). Epigenetic inheritance through sexual reproduction is still controversial; the stress-induced epigenetic state must be meiotically stable and survive epigenetic reprogramming during gametogenesis and seed development for the heritability of acquired resistance (Epi-bred plants; Figure 3) (Bilichak and Kovalchuk, 2016). Transgenerational memory of a stressor may be based on genomic regions that differ in their epigenetic state, known as epialleles. Epialleles are of great importance in plant breeding, especially under climate change conditions, as they may be used to develop new, flexible, and stress-responsive crops with enhanced stress resilience relatively quickly (Varotto et al., 2020) (Figure 3).

There are different strategic possibilities to explore the epigenetic potential of plants for breeding purposes. Utilizing epigenetic diversity associated with agronomically important traits inherent in natural or cultivated populations may be one way to enhance crop stress resilience. This may involve the epigenetic diversity of a population, including epialleles, heritable histone modifications (e.g., H3K9me3 and H3K27me3), or alterations in the regulatory system of the epigenetic mechanisms, which can be subjected to artificial selection similar to genetic alleles (Greaves et al., 2014; Varotto et al., 2020; Gallusci et al., 2023; Berger et al., 2024). This necessitates profiling the epigenome, including accessibility and modifications in the chromatin (DNA methylation and histone modifications) (Sánchez et al., 2016; Meller et al., 2018; Furci et al., 2019; Sampson et al., 2024), as well as

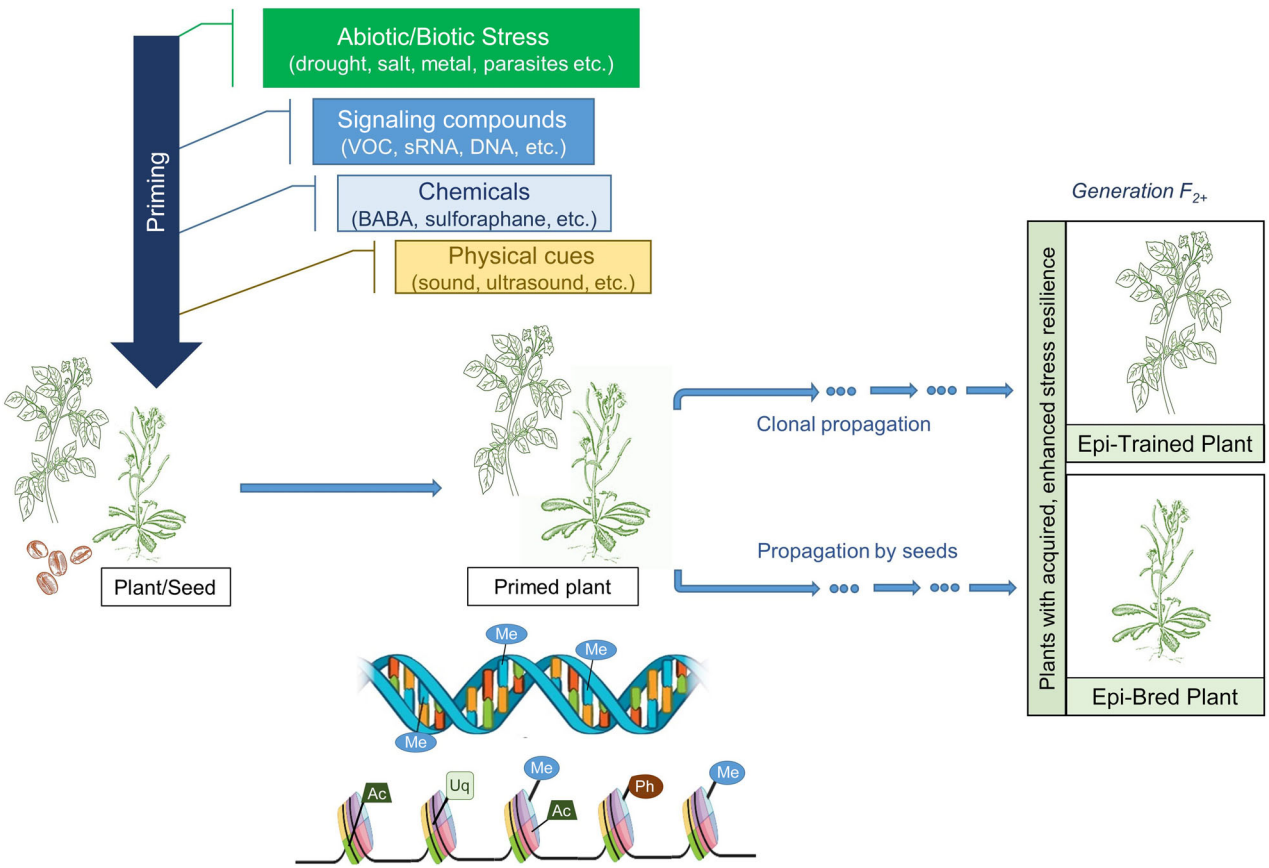

Figure 3. Priming-mediated modification of the plant epigenome for the production of epigenetically trained (Epi-Trained) or bred (Epi-Bred) plants

Transgenerational inheritance of stress memory, involving the transmission of epigenetic marks across generations, presents a novel opportunity in plant production and breeding. The mechanism of this transmission is influenced by the plant's mode of reproduction. *Epi-Trained Plants* (Asexual Propagation): in asexually propagated plants, stress-induced epigenetic states are passed on to the next generation via mitosis. This offers an innovative strategy to "train" parental plants, enhancing the tolerance of their clonal offspring to single or multiple stresses. *Epi-Bred Plants* (Sexual Reproduction): epigenetic inheritance through sexual reproduction requires the stress-induced epigenetic state to withstand epigenetic reprogramming during gametogenesis and seed development, allowing acquired resistance to be inherited by the progeny. This process relies on epialleles, which are genomic regions exhibiting heritable differences in their epigenetic state. These offspring are termed Epi-bred plants. VOC, volatile organic compound; sRNA, small RNA; BABA, β-aminobutyric acid; Me, methylation; AC, acetylation; Uq, ubiquitination; Ph, phosphorylation.

identifying regulatory RNA population, and creating of epigenetic databases.

Predicting the relationship between a phenotype and stable epigenetic variation(s), for example, deciphering the epigenetic alphabet (Gallusci et al., 2017; Guarino et al., 2022), may allow the use of epigenetic variants for breeding purposes by (de)activating epivariations of concern. This implies the artificial modification of the epigenome, either globally or targeted (Varotto et al., 2020; Gallusci et al., 2017, 2023). The use of chemical inhibitors of DNA methylation, for example, 5-azacytidine, may increase the variability of epigenetic variants; however, they may affect the methylation of multiple genes across the epigenome, also causing undesirable phenotypes. However, some chemical agents can be used for targeted modification of the epigenome. For example, BABA-induced resilience to stress against *Phytophthora infestans*, related to H3K4me2, H3K27me3, and DNA hypomethylation, was transmitted to offspring in potato (Meller et al., 2018; Kuznicki et al., 2019).

Unlike some chemicals that act genome-wide and non-specifically, and causing DNA hypomethylation, (e.g., 5-azacytidine, 5-aza-2′-deoxycytidine and zebularine) (Ogneva et al., 2019; Zhang et al., 2020; Li et al., 2021; Liang and Jiang, 2021; Liu et al., 2021a), genome-editing tools, like CRISPR (clustered regulatory interspaced short palindrome repeats), TALE (transcription-like effector), or ZFN (zinc finger nuclease) systems allow targeted, purposefully designed modification of the epigenome (Qi et al., 2023). These enable locus-specific modification of DNA methylation patterns and histone modifications (Bilichak and Kovalchuk, 2016; Waryah et al., 2018; Qi et al., 2023; Sampson et al., 2024). Veley et al. (2023) successfully applied ZFNs to improve cassava resistance against bacterial blight by using DMS3 (DEFECTIVE IN MERISTEM SILENCING 3) in the ZFN system. Thus, the methylation of the effector binding element of *SWEET10a*, a susceptibility gene of the plant, was modified, which led to hindering its expression and causing resistance to the bacterial disease. The development of the CRISPR/dead-(d)Cas9 system in epigenome editing is emerging (Sampson et al., 2024). Plant resistance to drought stress was improved in *A. thaliana* by the CRISPR/dCas9 system, for example, by fusing dCas9 with histone acetyltransferase 1 (Roca Paixão et al., 2019) and ROS1 demethylase (Devesa-Guerra et al., 2020). Although the CRISPR/Cas9 system is the leading technology in genome/epigenome--editing tools due to its operational simplicity, high efficacy and low cost, there are some limitations which need to be addressed for wider application (Qi et al., 2023; Raza et al., 2025). These include reducing off-target effects by improvement of Cas9, sgRNA (single guide RNA), or delivery methods, using gene editors acting without generating DNA double-strand breaks (DSBs) as reviewed elsewhere (Guo et al., 2023b). The effectiveness of the system was increased by applying aptamers, such as SAM (Synergistic Association Mediator) (Konermann et al., 2015) and SunTag (Papikian et al., 2019); strategies for improving the editing efficiency were recently reviewed in the study of Wang and Han (2024). Another bottleneck to the wider application of the gene-editing technology currently is not technical, but, as mentioned above, comes from the lack of extensive knowledge related to the relationship between the epigenome and the phenotype (Sampson et al., 2024). Machine learning (ML)- and artificial intelligence (AI)-driven models based on high-throughput phenotyping and omics data offer the potential to improve the prediction of interactions and relationships between epigenetics and stress tolerance in various crops.

THE USE OF AI AND ML IN PLANT EPIGENETICS

Approaches for epigenetic marks prediction

The epigenetics field is awash in data, presenting both a significant challenge and a transformative opportunity. Artificial intelligence is emerging as a powerful tool to navigate this "data deluge," enabling the extraction of relevant insights even from complex genomic–environmental interactions (GxE) (Butera et al., 2023; Boye et al., 2024). Traditional statistical methods, often hindered by the complexity, high dimensionality, and non-linearity of omics data, are increasingly being complemented—and sometimes surpassed—by AI models, particularly ML and deep learning (DL; a type of ML that uses neural networks) (Kang et al., 2022; The Business Research Company, 2025). For instance, while traditional statistical methods might identify DEGs or correlations between individual epigenetic marks and gene expression, AI models can integrate various omic data layers (e.g., genomics, transcriptomics, epigenomics and proteomics). Furthermore, AI can incorporate RNA and protein secondary or tertiary structures into these layers, which is challenging for traditional methods (Sun et al., 2021; Yu et al., 2022). Therefore, AI can significantly impact epigenetics by incorporating additional information layers into omics data sets.

At the same time, AI approaches come with various limitations. Understanding the strengths and limitations of each AI model helps researchers select the most suitable architecture. Supervised learning is one of the most widely used ML techniques in classification and prediction in epigenetics. In this approach, a model learns from labeled data to predict outcomes. Such ML models include Extreme Gradient Boosting (XGBoost) (Chen and Guestrin, 2016), linear or logistic regression (Olive, 2017), Support Vector Machines (SVMs) (Hosmer et al., 2013; Schölkopf and Alexander, 2022), Random Forest algorithms (Breiman, 2001), and Least Absolute Shrinkage and Selection Operator (LASSO) regression (Zemlianskaia et al., 2022). Linear or logistic regression techniques are commonly applied to examine the relationship between epigenetic features and phenotypic traits. Support Vector Machines are used to group samples based on epigenetic profiles (e.g., DNA methylation) or detect novel subgroups in the data (e.g.,

sample subtypes) (Fernández and Miranda-Saavedra, 2012). Random Forests rank the importance of various genomic features (e.g., specific methylation sites) in predicting phenotypic outcomes (Chen and Ishwaran, 2012). LASSO is used to identify the most significant epigenetic features (such as methylation patterns) associated with developmental stages (Brieuc et al., 2018). This technique divides the data set into k subsets, training the model on $k-1$ subsets and testing the remaining subset. This process is repeated multiple times to evaluate performance and robustness (Wong, 2015), to ensure that the model is well-generalized.

Epigenetics' complexity and high-dimensional nature (such as gene expression data, DNA methylation, or chromatin accessibility) often require unsupervised ML techniques to extract meaningful patterns and features (Arslan et al., 2021). Unlike supervised learning models that predict specific labels based on labeled data (e.g., control vs. treatment), unsupervised learning seeks to uncover hidden structures or relationships in unlabeled data (Bröker et al., 2024). It is particularly valuable for exploratory data analysis, enabling the discovery of hidden structures and generating novel hypotheses. Furthermore, it is useful for tasks like clustering and feature extraction. These approaches, to reduce complexity, often use dimensionality reduction algorithms. Principal component analysis (PCA) is one of the most widely used dimensionality reduction techniques (Ma and Dai, 2011), transforming the data into a set of orthogonal (uncorrelated) variables called principal components, which capture the maximum variance in the data. The first few principal components usually retain most information, and the rest can be discarded. t-Distributed stochastic neighborhood embedding (t-SNE) is a non-linear technique that reduces dimensions while preserving local structures (Linderman and Steinerberger, 2019). t-Distributed stochastic neighborhood embedding converts similarities between data points into probabilities and tries to match them in lower dimensions. Unlike PCA, t-SNE is more suitable for complex, non-linear data structures (e.g., network nodes). Uniform Manifold Approximation and Projection (UMAP) is similar to t-SNE but preserves data set local and global structures, constructing a graph to represent the relationships between points in high-dimensional space and then optimizing the layout in a lower-dimensional space (Armstrong et al., 2021). Uniform Manifold Approximation and Projection is often faster and more scalable than t-SNE while preserving a more global structure.

Regarding DL models, many can be applied in epigenetics, often in combination with dimensionality reduction techniques such as autoencoders. An autoencoder is an artificial neural network that learns to encode high-dimensional data into a lower-dimensional latent space, and then reconstruct the input from this representation, thereby capturing key features of the data (Zhou et al., 2018; Powadi et al., 2024). For example, Recurrent Neural Networks (RNNs) (Mienye et al., 2024) utilize memory mechanisms to process sequential data such as genomic sequences, but face limitations with long sequences. Recurrent Neural Networks are well-suited for processing sequential genomic data like DNA sequences, enabling predictions of methylation patterns or chromatin states, and gene expression prediction between labeled samples (e.g., stressed vs. non-stressed plants). Graph Neural Networks (GNNs) are well-suited for analyzing interconnected biological data, such as molecular interaction networks. Graph Neural Networks excel at identifying interactions between transcription factors, key DNA methylation sites, enhancers, and target genes, or analyzing Hi-C contact maps to predict chromatin architecture. Nevertheless, GNNs can be resource-intensive and face challenges regarding scalability (increasingly large graphs) and over-smoothing (node features averaging out, making their representations too similar) (Gamarnik, 2023; Du et al., 2024; Jiang et al., 2024). Convolutional Neural Networks (CNNs) effectively capture spatial hierarchies and patterns in grid-like data, effective for capturing spatial patterns in genomic data, and thus excel in tasks like identifying sequence motifs from Assay for Transposase-Accessible Chromatin using Sequencing (ATAC-Seq) data. Yet, CNNs are less suitable for sequential or non-spatial data and much less effective for long-range interactions, require substantial data for optimal performance, and may require careful tuning of filter sizes and layer depths to capture meaningful patterns (Koo and Eddy, 2019; Song et al., 2022; Mienye and Swart, 2024).

Approaches that align with the roles of epigenetic writers, readers, and erasers may yield further insights into epigenetic memory and phenotypes. Relevant DL models include Generative Adversarial Networks (GANs), which consist of two competing networks: a generator and a discriminator (Ghahramani et al., 2018). Just as the GAN generator produces realistic synthetic data, epigenetic writers establish marks on DNA or histones to encode cellular identity or memory. Generative Adversarial Networks are particularly valuable for data augmentation when working with limited data sets, as the generator's ability to introduce subtle changes can simulate how writers deposit diverse, context-specific epigenetic marks. The discriminator assesses the authenticity of generated data, analogous to how epigenetic readers interpret existing marks to influence gene expression. Readers evaluate whether a specific epigenetic signature corresponds to a functional cellular state, similar to the discriminator distinguishing real from synthetic data. Meanwhile, erasers act as regulatory elements that remove marks, much like how the discriminator penalizes unrealistic outputs, maintaining a balance in training. The adversarial nature of GANs reflects a broader tension between epigenetic stability (homeostasis) and flexibility (plasticity). However, GANs face challenges such as mode collapse and training instability, where the generator produces repetitive or low-quality outputs instead of exploring the full diversity of possible outcomes. This is especially problematic in epigenetics, where subtle molecular differences can drive highly diverse phenotypes (Yu et al., 2021; Oladayo Esan et al., 2023). Addressing these challenges may require advanced

GAN variants, such as Wasserstein GANs, unrolled GANs, or dynamic clustering frameworks (e.g., DynGAN) (Zou et al., 2023; Wang et al., 2023a; Luo and Yang, 2024). It is important to note that, despite their potential, direct applications of GANs in plant epigenetics have yet to be demonstrated.

A less complex model in DL is the Multi-Layer Perceptron (MLP). Multi-Layer Perceptrons are feedforward neural networks suitable for tasks such as regression, pattern recognition, and classification (Tripathi et al., 2022; Rashedi et al., 2024). While MLPs lack the architectural complexity of models like GANs, they offer clear advantages for modeling specific epigenetic features. For example, MLPs can predict gene expression from methylation profiles or classify plant cell types based on chromatin state data. However, MLPs are generally less effective at modeling complex data distributions or generating novel epigenetic profiles, and they struggle to capture intricate spatial or contextual dependencies. Still, MLPs have been successfully applied to predict exon positions in plant genomes from RNA-seq data (Jahedi et al., 2023). Although not directly focused on epigenetics, this approach could be adapted for analyzing epigenetic markers, such as DNA methylation or histone modifications, by leveraging high-dimensional plant genomic data sets.

Other DL approaches, such as Transformer models and Large Language Models (LLMs), may open new frontiers in epigenetics. Their ability to process massive data sets and capture long-range dependencies makes them well-suited for tasks such as integrating multi-omics information and generating data-driven hypotheses. Unlike earlier models that process data sequentially, Transformers analyze all input elements in parallel, significantly improving training speed and scalability (Wang et al., 2023b). Transformer-based models like Bidirectional Encoder Representations from Transformers (BERT) and Generative Pre-trained Transformer (GPT) have since been adapted for computer vision in tools like Vision Transformers (ViTs) (Wang et al. 2025). However, these models have high computational demands and require large training data sets, which may limit their use in resource-constrained research settings (Luo et al., 2023; Patwardhan et al., 2023; Zhang and Shafiq, 2024). Just as LLMs are trained on specialized language corpora, omics data sets offer a structured foundation for training models to interpret biological processes across multiple layers (Gao et al., 2024). These methods are particularly promising for interpreting ncRNA-seq data, and likely capture aspects of epigenetic regulation, enabling insights into cellular diversity and function. Although LLMs have not yet been directly applied to plant epigenetics, relevant tools and frameworks are beginning to emerge (Gao et al., 2024).

Deep Belief Networks (DBNs) are probabilistic generative models useful for unsupervised learning and feature extraction (Hinton et al., 2006; Li et al., 2025b). Deep Belief Networks discover hidden relationships between epigenetic marks (e.g., methylation and histone modifications) and gene expression without requiring pre-labeled data. Common performance measures employed in classification tasks that use balanced data sets for training are accuracy, sensitivity, specificity, and precision (Sokolova and Lapalme, 2009). Deep Belief Networks have been used for crop classification, pest prediction, and yield forecasting by extracting high-level features from agricultural data sets. DBNs could be adapted for analyzing epigenetic markers like DNA methylation or histone modifications in plants (Patel et al., 2024). Another similar technique, the Self-Organizing Maps (SOMs) (Javed et al., 2024), helps researchers uncover latent features, identify clusters, and model complex relationships in DNA methylation, gene expression, and histone modification data (Nikkilä et al., 2002). Like DBNs, SOMs have not been used in plant epigenetics (Yang, 2025).

The interpretability of complex AI models, such as supervised model architectures, poses a significant challenge in translating predictions into biological understanding. While these models offer high accuracy, understanding exactly why they make certain predictions (their interpretability) can be a challenge. The "black box" nature of some models makes it challenging to identify the precise biological mechanisms behind these predictions. Figure 4 outlines the analytical pipeline, which consists of three main steps: (i) data preprocessing with normalization and quality control; (ii) feature engineering with dimensionality reduction through PCA analysis and data imputation (a process used to fill in missing values); and (iii) model selection and training. In the same context, AI can also handle complex issues like microclimate variability across a field (Chen et al., 2024), which is increasing noisy patterns in traditional analyses.

Integrating epigenotypes to phenotypes: toward epigenetic ideotypes

Integrating phenotypes with epigenetic omics data is fundamental to develop robust crops across diverse environments – a concept known as "epigenetic ideotypes" (Donald, 1968). Large-scale imaging, facilitated by "plant phenomics" (i.e., the systematic study of phenotypes at scale), is often essential to validate subtle phenotypic effects arising from epialleles, which may be overlooked by traditional methods (Sheikh et al., 2024). Plant phenomics can be achieved through advanced sensors, offering real-time data and data sets with the depth and richness required to unlock the full potential of AI applications (Pasala and Pandey, 2020). This automated monitoring enhances the accuracy of field assessments and reduces labor costs, providing deeper insights into the complex interplay between epigenetic states and environmental conditions.

Machine learning models employed in phenomics include regularized linear regression, sometimes combined with LASSO for implicit feature selection (Liu et al., 2019b), and techniques like SVMs or Support Vector Regression (SVR) (Zhao et al., 2020b). Machine learning approaches, like SVR, could be valuable for modeling these modifications and their effects on gene expression. SVRs have been used for the analysis and modeling of genome prediction of quantitative

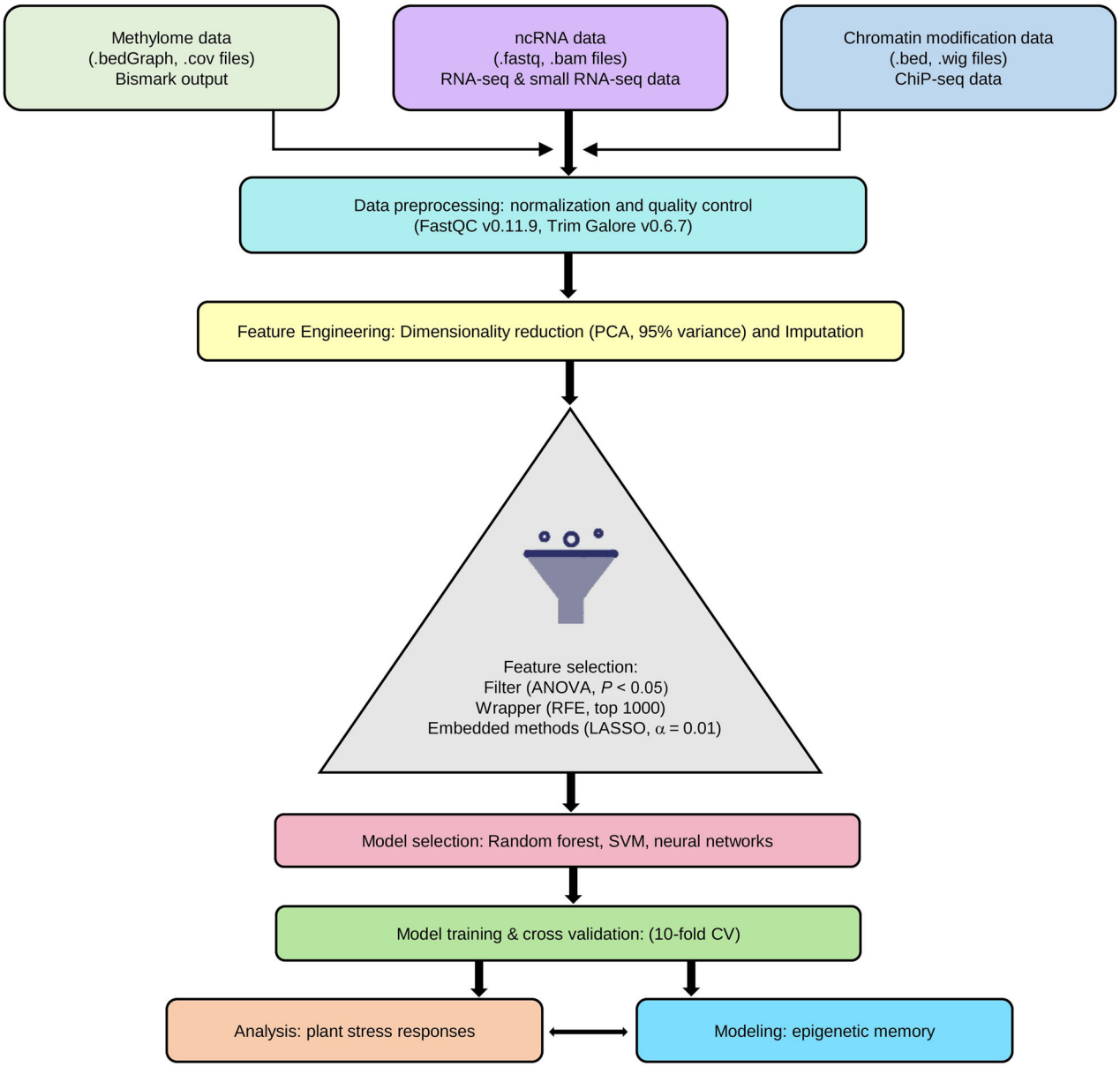

Figure 4. Machine learning pipeline for integrating and analyzing multi-omics epigenetic data in plant stress responses
This workflow outlines the steps involved in using machine learning to understand how epigenetic modifications relate to plant responses to stress. *I. Input and Preprocessing*: The pipeline begins with three types of omics data: DNA methylation profiles (methylome data), non-coding RNA (ncRNA) expression levels, and chromatin modification patterns. Raw data undergo quality control using FastQC and normalization with Trim Galore. *II. Feature Engineering and Selection*: to prepare the data for machine learning, feature engineering involves dimensionality reduction using principal component analysis (PCA), retaining 95% of the variance, and imputation to handle missing values. Feature selection employs a combination of three approaches: (i) Filter Methods: analysis of variance ($P < 0.05$) to identify statistically significant features; (ii) Wrapper Methods: Recursive Feature Elimination (RFE) to select the top 1,000 most informative features; (iii) Embedded Methods: Least Absolute Shrinkage and Selection Operator (LASSO) with $\alpha = 0.01$ for sparse feature selection. *III. Model Training and Evaluation*: the selected features are then used to train three machine learning models: Random Forest, Support Vector Machines (SVM), and Neural Networks. Model robustness is assessed using 10-fold cross-validation (CV). Random Forest is chosen for its ability to handle numerous features and evaluate feature importance. SVM is included for its effectiveness with high-dimensional and sparse data sets. Neural Networks are used to model complex, non-linear relationships inherent in omics interactions. *IV. Output and Analysis*: the pipeline culminates in two parallel, interconnected analyses: (i) Characterization of Plant Responses to Stresses: identifying key epigenetic features and their patterns associated with different stress responses and (ii) Modeling of Epigenetic Memory: predicting and understanding the epigenetic signatures that contribute to long-term stress memory. The outputs of these analyses can iteratively inform each other, leading to a deeper understanding of the complex interplay between epigenetics and plant stress responses.

effects (Long et al., 2011). By analyzing data sets from imaging platforms or sensor technologies, these ML approaches can help detect early stress indicators, including nutrient deficiencies, drought, or pest infestations (Singh et al., 2021). Other DL-related models, particularly GNNs and CNNs (LeCun et al., 2015), excel at extracting spatial hierarchies and patterns from image data relevant to plant phenotyping and microscopy analysis in epigenetics (Yamashita et al., 2018; Shibu and Salim, 2023). Machine learning holds substantial potential for the analysis of interactions between epigenetic, transcriptional and translational regulation. At the RNA-seq level, DL techniques can be employed to model highly complex RNA–protein interactions and their structural relationships (Sun et al., 2021; Townshend et al., 2021; Wei et al., 2022). Furthermore, recent studies have explored how DL can integrate multiple AI approaches to build more comprehensive predictive frameworks (e.g., Qin et al., 2025).

These capabilities are especially valuable in plant epigenetics, where stress responses involve multilayered and dynamic regulatory networks.

Multi-Layer Perceptron utilizes a classic feedforward neural network architecture, where each node in one layer is fully linked to all nodes in the subsequent layer. It is simple to implement and performs well with structured data, which makes it a common choice for applications like regression and classification tasks (Tripathi et al., 2022; Nisha et al., 2024). Transformers (Luo et al., 2023) have become state-of-the-art for sequence-to-sequence tasks due to their self-attention mechanisms that allow parallel processing and capture long-range dependencies. They were first created for natural language processing (NLP) tasks, as seen in models like BERT and GPT, and ViTs. In plant omics, Transformer architectures are being explored for sequence labeling tasks such as identifying *cis*-acting regulatory elements, predicting DNA methylation, and classifying ncRNA function across tissues and developmental stages. However, because of their high computing requirements and reliance on large data sets, their application in conditions of restricted resources can be difficult (Patwardhan et al., 2023; Zhang and Shafiq, 2024).

Recent applications of Transformer architectures in plant biology show promising results in image-based diagnostics and transcriptomic analyses. A notable example is the AISOA-SSformer model (Dai et al., 2024), which improved semantic segmentation of rice leaf diseases by integrating a hierarchical Transformer encoder with sparse parameter updating and an attention-based feature refinement mechanism. This architecture outperformed traditional convolutional and hybrid models on metrics like Dice coefficient and Mean Intersection over Union (MIoU) (Guindon and Zhang, 2017), particularly excelling in identifying disease-affected areas with fuzzy edges and complex backgrounds. Such advances underscore the growing relevance of Transformer models in agricultural AI applications and highlight their adaptability to irregular and heterogeneous biological data. In addition to improving large-scale image recognition tasks, Transformer-based models have recently been adapted for small-scale transcriptomic analysis. For example, Huang et al. (2025) introduced TransGeneSelector, a hybrid DL framework that combines a Wasserstein GAN with a Transformer network to mine key regulatory genes from limited RNA-seq data. Applied to *A. thaliana* under germination and heat stress conditions, the model demonstrated superior classification performance and accurately identified upstream regulatory genes, validated via reverse transcription – quantitative polymerase chain reaction (RT-qPCR). This approach addresses a common bottleneck in plant omics, limited sample sizes, and highlights the potential of Transformer models for extracting biologically meaningful features, even in data-constrained settings.

Understanding the strengths and limitations of each model can help researchers and practitioners make informed decisions and select the most suitable architecture for their specific tasks. Omics data sets, when formatted as sequential or structured inputs, can provide a robust foundation for training LLMs to interpret biological processes across multiple levels (Lam et al., 2024). Notable examples include clustering methods and manifold learning approaches, which reveal underlying non-linear patterns similar to those identified through PCA. These methods provide powerful tools for interpreting ncRNA-seq data and can likely also include epigenetic information, driving insights into cellular diversity and function. Approaches that fit the corresponding writers, readers, and eraser models may provide further insights into epigenetic memory and phenotypes.

Machine learning or DL approaches can surpass the limitations of traditional phenotyping methods, which often lack the capacity for deep data acquisition and capturing subtle phenotypic variations. Machine learning algorithms were applied to identify epigenetic markers associated with adaptive traits under selection during domestication processes. Studies have used ML approaches to analyze epigenetic changes, such as DNA methylation patterns associated with pathogen resistance (as a phenotype). For example, epigenetic markers were identified in maize for distinguishing active genes from pseudogenes based on DNA methylation profiles (Cembrowska-Lech et al., 2023; Sun et al., 2023). Yet, the application of these approaches, especially DL, remains limited in the plant epigenetic field.

Methylation dynamics in plant stress memory—insights from omics and ML

Moving forward, integrating extensive genome-wide data with multi-generational phenotypic data sets is a robust foundation for AI-driven predictive epigenomics (N'Diaye et al., 2020). Unlike traditional statistical methods, which often struggle to find patterns in the vast and complex data sets generated, AI excels at identifying subtle patterns and making predictions from these high-dimensional data sets (Xie et al., 2024). This capability is crucial for understanding the complex interplay of epigenetic marks in plant memory. Successful examples of AI-driven selection of methylation

dynamics in plant stress memory are rather limited. Yet, ML has successfully identified distinct methylation signatures associated with drought resistance in rice (Smet et al., 2023). Random Forests, as they combine the predictions of many decision trees (akin to a consensus of experts), are particularly good at assessing the importance of different features in the data, making them ideal for this type of analysis (Zhao et al., 2018). Machine learning has transformed DNA methylation studies by enabling precise identification and prediction of methylation signatures in diverse biological contexts (Mavaie et al., 2021). In plants, methylation changes at promoter and regulatory regions control stress-responsive genes, and ML models have been applied to identify genomic regions susceptible to methylation shifts under stressors, such as drought, heat, salinity, or pathogens (Mavaie et al., 2021; Rico-Chávez et al., 2022; Kimotho and Maina, 2024). N'Diaye et al. (2020) applied six ML algorithms and a deep neural network to predict tissue-specific gene expression in wheat (*Triticum aestivum* L.) using whole-genome bisulfite sequencing data. Their models achieved up to 81% accuracy, identifying promoter CG methylation as the most informative feature, and directly linking methylation patterns to gene expression.

Similarly, Wang et al. (2021a, 2021b) developed the Smart Model for Epigenetics in Plants (SMEP), a DL model capable of predicting multiple epigenetic marks, including DNA m^5C, RNA m^6A, and histone modifications, with ~80%–95% accuracy in rice, maize and *A. thaliana*. This model was experimentally validated using data from heat-treated rice seedlings, confirming predicted m^6A methylation changes post-stress. Common ML models like Random Forests and DL architectures have been effectively used to map methylation dynamics under varying levels and durations of stress, enabling identification of stress-associated epigenetic marks in rice and wheat (Wang et al., 2021a; Smet et al., 2023; Mansoor et al., 2024). In this framework, Random Forest classifiers further refine the analysis by distinguishing stress-adaptive genes and pinpointing key regulatory regions (Zhao et al., 2018). Moreover, unsupervised methods, particularly clustering and PCA, have been used to identify drought-responsive differentially methylated regions (DMRs), some of which were experimentally validated by bisulfite sequencing and functional assays, confirming their role in stress memory and potential transgenerational inheritance (Murmu et al., 2024). These findings resonate with the conceptual framework proposed by Galviz et al. (2022), who emphasized that stress responses and memory in plants unfold across interconnected spatial and temporal dimensions. Their "space-time biological stress concept" suggests that epigenetic marks, such as DNA methylation, can serve as molecular bridges between past stress events and future responses, enabling plants to recall and adapt to recurrent challenges. In rice, early hybrid ML–DL models demonstrate the ability to group DMRs associated with drought resistance and predict heritable epigenetic changes (Shaik and Ramakrishna, 2012).

In *Medicago ruthenica* (L.) Trautv. drought stress memory links to specific methylation patterns (hypomethylation) in genes like Chalcone Synthase (*CHS*) and Delta-1-Pyrroline-5-Carboxylate Synthetase (*P5CS*), validated through bisulfite sequencing and RT-qPCR (Zi et al., 2024). Machine learning models trained on similar methylome data sets identified conserved methylation signatures in root tissues that persist post-recovery, aligning with the sustained upregulation of stress-responsive genes (Champigny et al., 2020; N'Diaye et al., 2020; Zhang et al., 2024). Furthermore, CNN models accurately predicted epigenetic marks in rice (*Oryza sativa* L.), including DNA m^5C, m^6A, and histone marks like H3K4me3, H3K27me3, and H3K9ac (Rahman et al., 2021; Wang et al., 2021a). Yet, most applications remain focused on single-generation trait prediction, high-throughput phenotyping, genomic selection, and environmental modeling. The potential for leveraging AI to model transgenerational effects, such as epigenetic inheritance or long-term adaptation, remains largely unexplored. This is a promising frontier, and the field is only beginning to investigate these possibilities.

Regarding the single-cell level, recent advances in single-cell epigenomics have shed light on the cell-type-specific regulation of stress responses in plants. Nobori et al. (2025) combined single-nucleus RNA-seq and ATAC-seq (snMultiome) with spatial transcriptomics (MERFISH) to map immune responses in *A. thaliana* at single-cell resolution. This integrative approach led to the discovery of rare PRIMER cells, immune-primed cell states with unique chromatin accessibility and transcription factor motifs, revealing how epigenetic marks vary across cell types and spatial domains. By resolving transcription factor-accessible chromatin region-gene modules, the study demonstrated how immune memory and transcriptional responsiveness are encoded in distinct epigenomic profiles. Recent work by Schouveiler et al. (2025) outlined practical workflows for applying single-cell transcriptomics and chromatin accessibility assays in *A. thaliana* seeds, demonstrating how integration with spatial metabolomics can unravel tissue-specific regulatory networks involved in dormancy, germination, and early stress responses. These findings underscore the power of single-cell epigenomics in decoding the dynamic, multilayered regulatory mechanisms underlying stress memory in plants.

Beyond single-species studies, ML models trained on cross-species genomic data have shown the capacity to predict mRNA abundance and link sequence variation to gene activity. In *Populus balsamifera* L., DNNs—which can model highly complex non-linear relationships through multilayered learning—have demonstrated that traits in novel genotypes can be accurately predicted using a limited number of DNA methylation markers. This highlights the potential of AI to process high-dimensional epigenetic data and extract biologically meaningful relationships (Tahir et al., 2024). This approach effectively classified tissue types and geographic provenance and explained a significant portion of phenotypic variance in quantitative wood traits, based on

natural variation in DNA methylation. Additionally, ML techniques are increasingly applied to expression quantitative trait loci (eQTL) analysis, identifying associations between epialleles, memory formation, and adaptive behaviors (Zhao et al., 2023). These approaches could be further extended to investigate transgenerational epigenetic memory. Even in studies not directly applying ML, such as the identification of drought-induced DMRs in barley using Methylation-Sensitive Amplified Polymorphism (MSAP-seq) analysis (Xiong et al., 1999) (a PCR-based technique used to study DNA methylation patterns at specific CCGG recognition sites in a genome) the generated data (e.g., reversible methylation changes in genes like *HvP5CS1* linked to stress memory) is well-suited for ML algorithms. Approaches, such as Gradient Boosted Trees (GBT), to predict memory-associated methylation patterns (Li et al., 2022b), could be used.

Another aspect of stress memory relates to repeated stress exposures in one generation. This type of memory allows plants to "remember" an initial stress event during their development and respond more effectively to subsequent similar stresses later in the same generation. Somatic stress memory is mitotically inherited and typically lasts for a relatively short period without involving changes to the genetic sequence itself (Yadav et al., 2022; Kambona et al., 2023). Machine learning applications in crops like rice and wheat prioritize stable methylation mark identification associated with repeated stress cycles, which are more likely to contribute to heritable stress memory. For instance, studies have linked osmotic tolerance in rice seedlings to hypomethylation of *OsSOS1* and root-specific methylation loss under salinity stress (Yin et al., 2024). By integrating multi-omics data sets, ML models can prioritize specific loci, such as *OsNRAMP5*, for targeted genome editing using CRISPR technology to enhance crop resilience. In rice and wheat, ML-driven predictions of stable methylation marks following repeated stress exposure are guiding breeding efforts aimed at improving crop resilience to adverse environmental conditions (Benlioğlu et al., 2024; Yin et al., 2024). In rice, MSAP analysis revealed that drought-resistant varieties like Huhan-3 exhibit stable transgenerational inheritance of stress-induced hypermethylation loci, which correlate with improved drought tolerance across generations (Zheng et al., 2013). Machine learning-driven analyses of such data sets could effectively isolate stress memory-associated loci by filtering out stochastic methylation variations common in stress-sensitive varieties.

These advancements underscore the critical role of AI in deciphering the epigenetic basis of plant stress memory while mitigating the risk of over-generalization through rigorous experimental cross-validation (CV). However, we should note that there are also species-specific effects on stress memory. For example, research in *A. thaliana* utilizing whole-genome bisulfite sequencing has shown that many drought-induced methylation changes are temporary, with limited transgenerational inheritance (Ganguly et al., 2017). Here, ML classifiers were vital in distinguishing context-specific methylation from potential stress memory candidates, highlighting AI's ability to detect subtle yet biologically significant patterns within complex data sets. Furthermore, most crop methylation data are generated using bisulfite sequencing techniques rather than directly from ML models. Future research should, therefore, focus on integrating ML with robust wet-lab validation methods, such as CRISPR-edited lines, to effectively bridge the gap between prediction and practical application in breeding programs. It is also crucial to recognize tissue-specific variability, as highlighted by studies in maize that found minimal consistent stress-induced methylation changes. The analysis of extensive data sets generated from NGS and cutting-edge technologies like Oxford Nanopore, particularly when combined with high-resolution single-cell methylome analysis, is often complicated by the inherent challenge of integrating diverse data layers and the substantial variability of methylation patterns observed across different plant species, tissues, and environmental conditions (Omony et al., 2020; Agius et al., 2023). This limitation underscores the need for ML models that can accommodate such biological complexities to ensure accurate and relevant predictions. Looking ahead, promising future directions include the development of more interpretable AI models, such as those employing attention mechanisms or SHapley Additive exPlanations (SHAP) values (methods to understand what the AI is "looking at" when making predictions), exploring the transgenerational inheritance of epigenetic memory through ML-driven analyses, and creating standardized, high-quality multi-omics data sets to train more robust and generalizable models (Ibragić et al., 2025).

Non-coding RNAs in plant stress responses: integration of omics and ML for predictive insight

Non-coding RNAs contribute to plant stress memory by modulating gene expression before, during, and after stress exposure, ultimately equipping plants for future challenges (Yang et al., 2023; Gill et al., 2024). Advances in omics technologies, particularly RNA-seq, have enabled detailed profiling of ncRNA in different tissues and stress conditions, revealing how specific ncRNAs (miRNAs, siRNAs, and lncRNAs) are upregulated or downregulated in response to environmental cues (Nejat and Mantri, 2018), and that they consistently increase during repeated drought cycles, highlighting their role in building stress memory (Yan et al., 2019). Drought-responsive miRNAs can suppress genes linked to water loss (Wei et al., 2009; Ferdous et al., 2015; Akdogan et al., 2016), while some lncRNAs may activate genes related to osmotic stress via interactions with chromatin-modifying complexes (Kim, 2021; Yang et al., 2023). Other miRNAs, such as those targeting pathogen resistance genes, contribute to plant immunity (Luo et al., 2024).

Despite recent advances, the functions of many ncRNAs remain poorly understood. Machine learning approaches have greatly promoted functional predictions of ncRNA based on the analysis of sequence motifs, expression dynamics and gene networks. Artificial intelligence can predict the missing landscapes of ncRNA roles from sequence

motifs, gene interactions, and expression profiles, uncovering functional relationships between ncRNAs and stress (Rincón-Riveros et al., 2021). Pradhan et al. (2023a) developed ASLncR, an SVM model trained on *k*-mer features, which predicts stress-responsive lncRNAs with 76.2% accuracy. In a related study, ASmiR (Pradhan et al., 2023b) used pseudo-K-tuple nucleotide composition to identify stress-responsive miRNAs with over 90% accuracy. Similarly, Kumar Meher et al. (2022) built SVM-based models to classify pre- and mature miRNAs with test accuracies between 62% and 69%, available via ASRmiRNA.

Unsupervised learning techniques like *k*-means, hierarchical clustering and PCA have been used to group ncRNAs based on expression similarity across stress conditions, revealing coordinated regulatory modules and shared functional responses, even in ncRNAs with unknown targets (Chen et al., 2019b; Chang et al., 2022). Additionally, CNNs and SVMs identify sequence motifs or structural features, aiding in the classification of ncRNAs into functional groups like miRNAs, siRNAs, or lncRNAs (Rincón-Riveros et al., 2021; Mathur et al., 2024). Machine learning models also assess expression stability across stress cycles, enabling the accurate identification of ncRNAs involved in stress memory and identifying targets for modifications (Yadav et al., 2024). Random Forest models, such as GENIE3, were effective in identifying lncRNAs that regulate resistance to significant plant pathogens like *Phytophthora infestans* in potatoes (Cao et al., 2021). Integrating ncRNA data with transcriptomic and epigenomic profiles enabled ML models to map ncRNA interactions within gene networks, offering insights into their roles in stress responses (Pradhan et al., 2023a). For example, an ML model predicted interactions between lncRNAs and miRNAs based on sequence and interaction profile similarity (Cai et al., 2022). Furthermore, examining ncRNA expression across tissues and stress scenarios revealed their broader role in plant defense, highlighting key regulatory ncRNAs, such as miRNAs, that enhance plant immunity by targeting pathogen resistance genes (Luo et al., 2024).

Meanwhile, DL models have been explored to predict interactions between lncRNAs and chromatin remodeling complexes, clarifying how ncRNAs change gene expression through chromatin dynamics (Tabe-Bordbar and Sinha, 2023). This study retrained ML models such as CPAT, PLEK, and LncFinder using plant-specific data sets to improve the identification of lncRNAs involved in chromatin remodeling and epigenetic regulation. The ensemble approach combining CPAT–plant and LncFinder–plant achieved higher precision in identifying plant lncRNAs across multiple species (Tian et al., 2024). More integrative models are emerging. Recent studies have applied ML approaches, such as SVM and Random Forest, to predict and analyze regulatory RNAs involved in stress-responsive networks (Rico-Chávez et al., 2022; Pradhan et al., 2023a). Similarly, Vakilian (2020) employed Gaussian SVM regression to predict miRNA responses to drought, salinity, heat, and cold stress in Arabidopsis, achieving high predictive accuracy ($R^2 = 0.96$) and identifying key stress-associated miRNAs (miR-169, miR-159, miR-393, and miR-396). Beyond immediate stress responses, ncRNAs also participate in plant stress memory, modulating gene expression before, during and after stress episodes, thereby enhancing adaptive preparedness. Recent RNA-seq studies have proposed the expression stability of specific miRNAs as a marker for stress memory (Yang et al., 2023; Gill et al., 2024). Machine learning models have been developed to assess ncRNA expression patterns in successive stress events, identifying predictive features linked to adaptive responses and guiding the selection of genetic targets for resilient crop development (Yadav et al., 2024).

Lastly, the integration of ncRNA data sets with transcriptomic and epigenomic profiles enables the mapping of ncRNA-regulated gene networks. This systems-level view, supported by ML tools, provides mechanistic insights into how ncRNAs orchestrate complex stress responses (Tabe-Bordbar and Sinha, 2023; Pradhan et al., 2023a). Together, these advances pave the way for predictive, experimentally informed, and application-ready research on the involvement of ncRNAs in crop stress resilience. However, such predictions often require experimental validation to confirm their biological relevance. Consequently, future research should focus on techniques such as CRISPR/Cas9 to manipulate ncRNA expression or their networks, assessing the impact on plant stress memory and adaptation. Long-term studies are also needed to track ncRNA-mediated memory responses across multiple generations and under varying environmental conditions. Research should prioritize developing and applying precise techniques, such as single-cell RNA-seq and functional assays, to validate ncRNA targets and their functional relevance. Additionally, standardized protocols for ncRNA annotation and expression analysis are needed to improve data comparability across studies, ensuring robust and reproducible findings.

Chromatin modifications and stress adaptation: decoding the complexities with ML

In addition to DNA methylation, histone methylation and acetylation are pivotal epigenetic modifications which serve as molecular switches orchestrating plant stress memory, a crucial mechanism for survival and adaptation (Sharma et al., 2022; Gallusci et al., 2023). These dynamic chromatin marks precisely control the accessibility of stress-responsive genes, ensuring their timely activation or suppression upon subsequent stress exposure. The application of ML methods, leveraging the power of chromatin immunoprecipitation sequencing (ChIP-seq) data, has significantly enhanced our ability to predict these vital histone marks associated with various environmental stressors (Wu et al., 2019; Li et al., 2022c; Heping et al., 2024). Using ChIP-seq for stress-exposed plants reveals how histone modifications respond to environmental cues. Specific histone marks often accumulate at the promoters of stress-responsive genes and facilitate their rapid activation (Ueda and Seki, 2020), while repressive modifications target regions that need to be silenced to

conserve energy and resources (Yung et al., 2021). Large-scale ChIP-seq data sets are invaluable for identifying stress-responsive chromatin regions. When combined with transcriptomic and methylome profiles, they provide a comprehensive view of the role of chromatin in stress responses, revealing regulatory loci that may serve as targets for crop improvement.

Machine learning models help manage the complexity of chromatin modification data, particularly in identifying histone marks linked to plant resistance to stress. Trained on ChIP-seq data, these models can predict histone marks associated with plant stress resilience or susceptibility to specific environmental stressors like drought, salinity and plant pathogens (Wu et al., 2019). They examine features such as genomic locations, enrichment levels, and correlations with gene expression to clarify the impact of chromatin dynamics in stress adaptation. In addition to individual histone modifications, ML approaches can also model interactions among chromatin marks and other epigenetic layers, including DNA methylation and ncRNA activity, to create a systems-level understanding of chromatin function (Roychowdhury et al., 2023). Analyzing time-course ChIP-seq data from plants subjected to repeated stress cycles enables AI models to dissect the temporal dynamics of chromatin modifications and pinpoint those specifically associated with memory formation. These models can also identify critical chromatin regions essential for long-term plant memory (Piecyk et al., 2022; Peng and Rajjou, 2024). Beyond individual histone modifications, ML approaches are increasingly used to investigate the complex interactions among various chromatin marks and other epigenetic elements, including DNA methylation and ncRNA (see below) activity (Roychowdhury et al., 2023). Other approaches could also boost the identification of epigenetic marks, such as the SMART approach, which includes histone modifications (Wang et al., 2021b). Chromatin modifications, particularly histone methylation and acetylation, contribute to the establishment of stress memory by preserving specific marks at genomic loci after stress exposure, enabling plants to "remember" past conditions and respond quickly upon re-exposure (Sharma et al., 2022; Gallusci et al., 2023). By modulating accessibility to stress-responsive genes, chromatin marks ensure these genes are readily activated or suppressed upon re-exposure. Recent studies have shown that ML models can successfully detect memory-associated histone modifications. By the analysis of time-course ChIP-seq data from plants subjected to repeated stress, these models can identify histone marks likely to function as memory indicators and pinpoint chromatin regions involved in plant stress adaptation (Piecyk et al., 2022; Peng and Rajjou, 2024). Smart Model for Epigenetics in Plants, described by Wang et al. (2021a, 2021b), was also trained on ChIP-seq data to predict histone marks such as H3K27me3, H3K4me3, and H3K9ac in rice. Wu et al. (2019) used a combined ChIP-seq and RNA-seq ML framework to predict drought-responsive histone patterns in *A. thaliana*, validated via ChIP-qPCR. Similarly, Peng and Rajjou (2024) applied DL to tomato time-course ChIP-seq data and identified H3K27me3 changes associated with heat memory genes, confirmed through RT-qPCR and phenotypic assays.

Yet, we are far from reaching a direct application of such models to integrative epigenetics but these studies demonstrate how AI has the potential to effectively pinpoint chromatin-based memory mechanisms. In the future, these approaches may support precision breeding and genetic engineering strategies aimed at improving crop resilience through the targeted manipulation of chromatin states. Furthermore, the same limitations mentioned above apply here for the additional marks on histones.

Epitranscriptomics and plant stress memory

Beyond DNA and histones, epitranscriptomics, the study of post-transcriptional RNA modifications, is increasingly recognized as a dynamic regulatory layer, critically influencing plant stress responses and memory. Modifications such as N6-methyladenosine (m^6A), pseudouridylation (Ψ), m^5C, and RNA editing affect RNA stability, splicing, translation, and interactions with RNA-binding proteins, enabling the fine-tuning of gene expression for effective adaptation to environmental stresses (Shoaib et al., 2022; Cai et al., 2025). Recent research indicates that RNA modifications contribute to plant stress memory by stabilizing stress-responsive transcripts and priming molecular pathways for future stress encounters (Liu et al., 2024), influencing transcript stability and translation efficiency under stress (Liu et al., 2024; Dobránszki et al., 2025; Kutashev and Moschou, 2025).

Among over 170 identified RNA modifications, m^6A is the most abundant and best-characterized internal mark in eukaryotic mRNAs, including those of plants (Hu et al., 2022). m^6A is deposited by "writer" complexes like MTA ((N(6)-adenosine-methyltransferase MT-A70-like), MTB (METTL14 human homolog protein) and FIP37 (FKBP12-interacting protein), removed by "erasers" such as the ALKBH (AlkB Homolog, Histone H2A Dioxygenase) proteins, and interpreted by "readers" with YTH-domains like ECT2, ECT3, and ECT4 (evolutionarily conserved C-terminal region 2, 3 and 4) (Liang et al., 2020; Shen et al., 2023). m^6A plays a multifaceted role in the regulation of mRNA splicing, export, stability, decay, and translation efficiency. These processes are central to transcriptomic reprogramming under stress, enabling rapid and reversible adjustments in gene expression. Importantly, m^6A marks often accumulate near stop codons and in 3′ untranslated regions (3′ UTRs), a spatial pattern associated with increased transcript stability and translational regulation (Liang et al., 2020; Shen et al., 2023). Transcriptome-wide studies in wheat under drought stress revealed that m^6A abundance positively correlates with mRNA levels of key stress-responsive genes. This response involved upregulation of the m^6A reader *ECT9* (gene encoding YTH-domain-containing family protein), which promotes drought tolerance, and downregulation of the eraser *ALKBH10B* (Pan et al., 2024). Similarly, in *A. thaliana*, the demethylase *ALKBH10B*

fine-tunes mRNA stability during drought, modulating decay rates of stress-inducible transcripts (Han et al., 2023). In addition to immediate stress responses, m^6A methylation also contributes to transcriptional memory and stress imprinting. In rice, high-resolution mapping showed dynamic shifts in m^6A deposition during repeated stress exposures with conserved 3′ UTR sites linked to memory-like expression patterns (Wang et al., 2024). Recent research by Li et al. (2025a) further confirmed the role of the m^6A writer *MTA1* in the regulation of seed germination and salt stress response in rice, linking m^6A hypomethylation to altered expression of key stress-responsive genes. These findings align with evidence in *A. thaliana* and *O. sativa* demonstrating that stress-induced m^6A methylation enables the stabilization or rapid re-induction of specific transcripts, potentially acting as reversible molecular imprints that sensitize plants to future environmental challenges (Hasan et al., 2024; Cai et al., 2025). Importantly, m^6A-mediated regulation functions alongside other RNA modifications such m^5C and Ψ, which are increasingly recognized for their roles in stress adaptation. These modifications exhibit cell-type specificity and context-dependent behavior, adding to the regulatory complexity. Emerging evidence suggests intricate crosstalk between sRNAs and lncRNAs, supporting a multilayered epitranscriptomic network (Statello et al., 2021).

The large data sets generated by epitranscriptomic studies (e.g., m^6A-seq and MeRIP-seq) present a significant opportunity for AI analysis, which can uncover patterns and dynamics that are difficult to manually interpret. The Plant Epitranscriptomic Analysis (PEA) toolkit is a notable example. It is an integrated RML toolkit specifically designed for plant epitranscriptome analysis, including the prediction of chemical modifications of RNA (CMRs) such as m^6A. Plant Epitranscriptomic Analysis employs ML technologies—specifically, the Positive Samples Only Learning algorithm—for transcriptome-scale prediction of CMRs in plants. Plant Epitranscriptomic Analysis has been applied to *A. thaliana* and demonstrated high sensitivity and specificity for m^6A prediction, outperforming existing predictors (Zhai et al., 2018). Other ML models, such as m^6A pred, predict m^6A sites across the transcriptome with $>90\%$ accuracy using sequence features and contextual information (Taguchi, 2023).

Machine learning models can be combined in this context with DL models, like RNNs and Transformers, to capture the temporal dynamics of RNA modifications during stress recovery. For example, RNNs trained on time-series m^6A data from heat-stressed tomato predicted modification "hotspots" on Heat Shock Protein (HSP) transcripts critical for thermotolerance (Vakulenko and Grigoriev, 2021). Similarly, DL frameworks like epitranscriptome analysis using nanopore sequencing (EpiNano), used with nanopore sequencing data, can simultaneously detect multiple RNA modifications. EpiNano is a computational tool designed to detect RNA modifications, particularly m^6A, from nanopore data using a pre-trained ML model to identify modified bases by analyzing "errors" (Shen et al., 2023). Integrating epitranscriptomic data with epigenetics, transcriptomics, and proteomics using ML frameworks reveals how RNA modifications contribute to gene expression networks under stress.

Artificial intelligence/ML tools accelerate the discovery of modification–function relationships and offer predictive insights into plant resilience mechanisms. Integrating epitranscriptomics with field phenotyping and genome editing holds promise for engineering climate-resilient crops. Deciphering this complexity is a major challenge due to the isoform diversity and dynamic nature of RNA modifications. As a result, AI and ML approaches have become essential. Tools such as 6mAboost, iRNA-methyl, and DL models trained on plant-specific data sets are advancing the prediction of modification sites, functional annotation, and integration with multi-omics stress response networks (Figure 5) (Acera Mateos et al., 2023). These tools enable the identification of stress-specific epitranscriptomic signatures and support the construction of dynamic regulatory models. In this context, recent advances in multi-epiomics, integrating epigenomics, epitranscriptomics, and epiproteomics (protein isoforms and their modifications in the context of epigenetic regulation), offer a powerful framework for decoding stress-responsive regulation and phenotypic plasticity with promising implications for crop resilience and sustainable agriculture (Miglani and Kaur, 2025). However, several challenges remain. Current methods for mapping RNA modifications (e.g., MeRIP-seq) lack single-nucleotide resolution (Zhong et al., 2023). While nanopore sequencing shows promise, ML-driven base calling improvements are still needed for higher accuracy (Liu et al., 2021b). Moreover, a holistic understanding of plant stress memory mechanisms requires combining epitranscriptomic insights with DNA methylation and histone modification data (Hu et al., 2022).

Altogether, epitranscriptomics represents a promising frontier in understanding how plants perceive, encode, and recall stress stimuli. When integrated with DNA methylation, histone modifications, ncRNAs, and chromatin remodeling, RNA modifications provide a more holistic view of plant stress memory systems. These regulatory layers converge into an integrated epigenomic landscape that coordinates transcriptional, post-transcriptional, and chromatin-level modifications, facilitating adaptive stress responses and long-term molecular imprinting. Future research should address these challenges and explore applications such as CRISPR-based epitranscriptome engineering.

Current limitations in AI applications to plant epigenetics

Artificial intelligence and ML offer powerful tools for the interpretation of complex epigenomic data sets, but several limitations still hinder their effective use in researching plant stress memory. A major concern is data set bias, as most available plant epigenetic data are derived from model species. This taxonomic imbalance limits the generalizability of AI models to different crops and wild species, many of which may possess distinct epigenetic architectures and stress response mechanisms (Richards et al., 2017). The temporal dynamics of epigenetic changes introduce an additional layer of complexity. In the context of stress memory, current AI approaches often fail

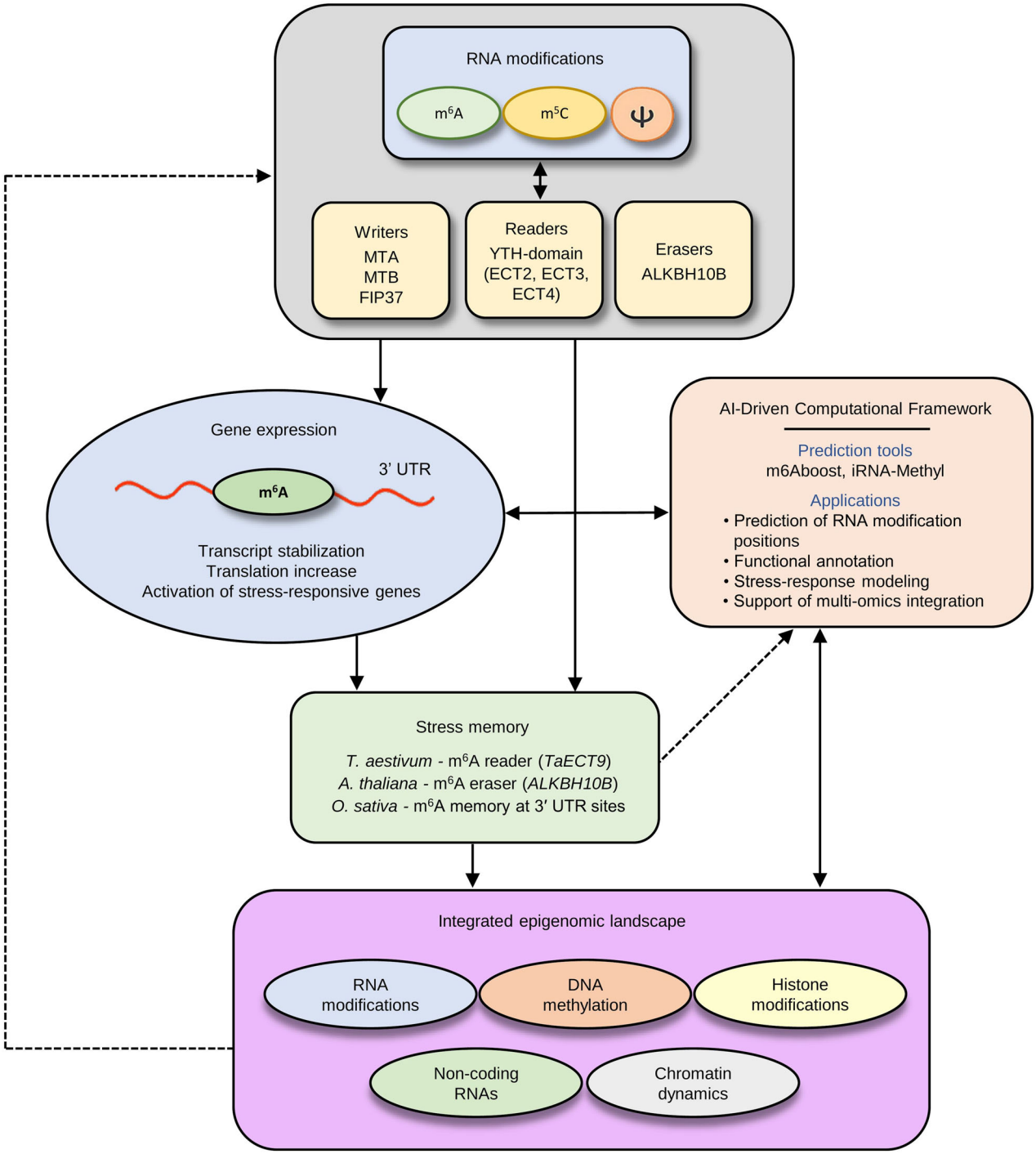

Figure 5. Integration of RNA modifications in plant gene expression, stress memory, and artificial intelligence (AI)-driven multi-omics frameworks

This figure illustrates how RNA modifications, specifically N6-methyladenosine (m^6A), 5-methylcytosine (m^5C), and pseudouridine (Ψ), influence gene expression and contribute to stress memory in plants. RNA Modifications and Gene Expression: these modifications generally enhance transcript stability and translation, particularly when located in the 3′ UTR (untranslated region), leading to the activation of stress-responsive genes. The deposition of these modifications is mediated by "writer" proteins (e.g., MTA, MTB, FIP37), their recognition by "reader" proteins (e.g., YTH-domain proteins ECT2–ECT4), and their removal by "eraser" proteins (e.g., ALKBH10B). Role in Stress Memory: studies in *Triticum aestivum* (wheat), *Arabidopsis thaliana*, and *Oryza sativa* (rice) have shown that persistent or recurrent m^6A marks, particularly at 3′ UTR sites, are involved in plant stress memory. AI-Driven Multi-Omics Framework: an AI-driven computational framework, utilizing tools such as 6mAboost and iRNA-Methyl, facilitates the prediction of RNA modification sites and their functional annotation. This framework enables stress response modeling and the integration of RNA modification data with other multi-omics data sets. Diagram key: solid arrows represent molecular pathways, while dashed arrows indicate feedback loops and computational inferences.

to capture the dynamic nature of epigenetic modifications across different stress exposure timepoints, recovery phases and transgenerational inheritance. Existing models still treat epigenetic marks as static features, overlooking their regulation and plasticity during plant development and across generations (Hemenway and Gehring, 2023). As mentioned above, another major problem is the interpretability of models, particularly for DL approaches that often operate as "black boxes". Such models may achieve high predictive accuracy, but they typically offer limited transparency, making it difficult to trace the rationale behind their predictions. The resulting opacity poses a barrier to uncovering causal links between specific epigenetic modifications and stress memory phenotypes, one of the primary goals in this field of research (Hemenway and Gehring, 2023; Qamar and Bawany, 2023).

Ecological relevance remains a major limitation in current AI applications to plant stress research, largely due to the scarcity of multi-stress data sets. In natural settings, plants often encounter simultaneous or sequential stresses (Georgieva and Vassileva, 2023), but most AI models are trained on simplified single-stress data derived from controlled environments. This simplification limits the capacity to capture the complex crosstalk and dynamic regulation of stress responses. Moreover, most phenotyping studies, including those using advanced ML-based imaging systems, are typically conducted in greenhouse conditions that fail to replicate the complexity and variability of field environments (Singh et al., 2021). At the same time, high-throughput phenotyping platforms generate vast heterogeneous data sets that are difficult to integrate, reducing the ecological interpretability of ML analyses (Gill et al., 2022; Kim et al., 2024). Technical challenges also arise in the integration of diverse epigenomic layers (methylome, chromatin accessibility and histone modifications) in different temporal and spatial scales. Many existing algorithms perform well on isolated omics layers, but falter when tasked with multi-omics integration, which is essential for modeling the mechanisms of stress memory. In addition, the high dimensionality of epigenomic data, combined with the small sample sizes typical of plant studies, increases the risk of overfitting and statistical noise. Cross-species prediction remains particularly problematic due to fundamental differences in genome architecture, methylation patterns and regulatory networks (Lämke and Bäurle, 2017). Transfer learning approaches show promise, as demonstrated in studies predicting gene function between *A. thaliana* and tomato, but require careful adaptation to account for evolutionary divergence in epigenetic mechanisms (Singh et al., 2021), which complicates the translation of findings from model species to agronomically important crops (Moore et al., 2020).

Finally, benchmarking is complicated by the absence of standardized data sets and evaluation metrics specific to plant stress memory research (Salai and Ramapuram, 2024), making it difficult to objectively compare model performance and establish best practices in this rapidly evolving field.

In summary, ML approaches hold great promise to uncover the epigenetic foundations of plant stress memory. To consolidate current knowledge on the molecular components involved in plant epigenetic regulation under environmental stress, Table 1 presents an overview of key genes and epigenetic marks associated with transgenerational memory. Each entry includes the type of epigenetic modification, commonly used detection techniques, and relevant AI-based tools for data analysis. Certain tools have been directly applied in the cited studies; others are suggested based on their compatibility with the corresponding data types. To facilitate interpretation, the tools mentioned in Table 1 are further described in Table S1, which provides their core functions and key references. However, current limitations in data availability, model interpretability, temporal modeling and cross-species applicability must be addressed. Integration of multi-omics data (DNA methylation, ncRNAs and chromatin modifications) via interpretable AI frameworks will be key for the identification of adaptive epigenetic markers, which could advance breeding and genetic engineering strategies and lead to the development of stress-resilient crops essential for sustainable agriculture in changing climates.

CONCLUSIONS

Modern agriculture faces two critical challenges: rapid increase in the worldwide population and climate change. The increasing demand for food necessitates enhanced agricultural productivity. However, this increase cannot be achieved due to intensified anthropogenic activities that pose environmental risks, such as water pollution, soil degradation and elevated greenhouse gas concentrations. Indeed, it is urgent to develop precision agriculture methods for rapid and cost-effective monitoring of crop health (Padhiary et al., 2024). These methods can significantly reduce the dependency on phytochemicals and excessive irrigation while sustaining crop yield. Crops are frequently exposed to multiple cross-stresses, a situation exacerbated by global climate change, impacting production yield and quality and consequently threatening food security (Basso et al., 2024). However, plants are constantly evolving to refine their defense mechanisms and resilience, orchestrated by the interplay of their genetics, biochemistry, and physiology (Mishra et al., 2024; Dobránszki et al., 2025). Beyond immediate responses to adverse conditions, plants acquire and accumulate epigenetic changes that are transferred or inherited transgenerationally to their progeny (Gallusci et al., 2023; Guarino et al., 2024). This molecular memory developed during and in response to the stress suffered by previous generations primes their offspring to respond and adapt to the same stress more effectively than other plants that have not gone through the same experience (Guarino et al., 2022; Gallusci et al., 2023). Innovative approaches are needed for the early identification of abiotic and biotic stressors directly in the field, using portable and user-friendly instruments. Simultaneously, developing climate-smart cultivars remains a primary goal in breeding programs. Genomic selection using high-throughput

Table 1. Key genes/epigenetic modifications involved in transgenerational memory—detection techniques and AI-based predictive tools

Key genes or epi-marks	Type of epigenetic modification	Molecular detection techniques	Reference	AI-based tool for analysis
FORGETTER 1 (FGT1)	Chromatin modification	ChIP-seq	Friedrich et al. (2019)	DeepHistone, ChromHMM
DDM1	Chromation modification	ChIP-seq	Osakabe et al. (2024)	DeepMod, EpiPredictor
MET1/2	DNA methylation	WGBS or methylation-specific PCR	Yang et al. (2020)	**Methyl-IT***, MethyQA
DRM1/2	DNA methylation	WGBS or methylation-specific PCR	Kinoshita and Seki (2014)	Methyl-IT, Methylpy
NREP1	DNA methylation	WGBS or methylation-specific PCR	López Sánchez et al. (2016)	MethylSeekR, DeepCpG
H3K4 and H3K27	Histone trimethylations	ChIP-seq and RNA-seq	Zha et al. (2021)	ChromHMM, Epic2
H3K4me2/3	Histone demethylation	ChIP-seq, ChIP-PCR, and RNA-seq	Hou et al. (2015)	DeepHistone, ChroModule
HDA6	Histone deacetylation	ChIP-PCR and RNA-seq	Wang et al. (2017)	**DESeq. 2***, DiffBind
H3K36	Histone methylation	ChIP-PCR	De-La-Peña et al. (2012)	Chromoformer, DeepHistone
H3K14	Histone acetylation	Western blot and HAT assay	Dubey et al. (2019)	DeepHistone
CHR5	Chromatin remodeling	ChIP and MNase-seq	Zou et al. (2017)	NucleoATAC, DANPOS
lncRNAs	Genetic and epigenetic effects	RNA-seq	Maleki et al. (2025)	PLncPRO, LncADeep
m^6A of multiple mRNAs	mRNA methylation and post-transcriptional regulation	RNA-seq, m^6A-RIP-seq, GMUCT-seq, RT-PCR and dot blot	Prall et al. (2023)	**MACS2***, **DESeq. 2***, m6Anet
m^5A of multiple mRNAs	DNA and RNA methylation	m^5C-RIP-seq and RNA-seq	Cui et al. (2017)	iRNA-m^5C, m^5UPred
miRNAs and phasiRNAs	DNA methylation	RNA-seq and methylome	Romero-Rodríguez et al. (2023)	miRDeep-P2, PHASIS

Note: The references cited provide the original identification or functional characterization of the listed genes or epigenetic marks. Bolded AI tools marked with an asterisk (*) have been used in the cited studies; the remaining tools are suggested based on compatibility with the data types generated in these papers.

Abbreviations: AI, artificial intelligence; ChIP-seq, chromatin immunoprecipitation and sequencing; ChIP-PCR, chromatin immunoprecipitation-polymerase chain reaction; GMUCT-seq, genome-wide mapping of uncapped and cleaved transcripts by sequencing; HAT assay, histone acetyltransferase assay; MNase-seq, micrococcal nuclease digestion combined with high-throughput sequencing; m^6A-RIP-seq, m^6A RNA immunoprecipitation followed by high-throughput sequencing; m^5C-RIP-seq, m^5C RNA immunoprecipitation sequencing; RNA-seq, RNA sequencing; WGBS, whole-genome bisulfite sequencing.

genotyping integrated with sensor-phenomics, speed breeding and digital twin technologies represents the forefront of modern crop breeding. Another emerging frontier is the development of virtual systems employing advanced software adjustments and network support to optimize crop productivity by simulating environmental conditions and agronomic treatments, providing valuable insights for decision-making. However, implementation of such integrative approaches remains hard for breeders and small- and medium-sized enterprises due to their complexity. Cyber-agricultural systems (CAS) could be designed to mitigate the negative effects of climate change and meet the increasing food demand through ultra-precision agriculture (Sarkar et al., 2024). These systems may integrate: (i) innovative approaches such as phenotyping to gather detailed crop data; (ii) modeling (advanced breeding methodologies to predict crop performance and implementation); and (iii) decision-making tools to optimize breeding and agricultural management. CAS will optimize agronomic treatments at both plant and field levels, replacing heavy machinery with smaller, lightweight, multifunctional platforms. This ultra-precision approach promises higher scalability, enhanced functionality and efficient management with reduced operational costs due to enhanced resilience to climate extremes and increased autonomy and profitability.

Enhancing our understanding of the relationship between this stress memory and its implications for the plant phenotype and agronomic performance through the identification of epigenetic marks will enable the implementation of biotechnological tools in plant breeding and genetic engineering through the (de)activating epialleles associated with desirable traits (Sampson et al., 2024). The effective identification of these marks is highly reliant on experimental plans that use multi-omic approaches (such as stress and non-stress bioassays in plants, DNA and RNA methylome, RNA and ncRNA transcriptome, chromatin status, histone marks, and plant phenomics), in which AI based on ML and DL may play a

prominent role in identifying plant memory molecular patterns in large-scale data sets (Heping et al., 2024; Peng and Rajjou, 2024; Yadav et al., 2024). With these multi-omics data sets, systematic AI approaches are applied for data preprocessing (quality control, data sufficiency, and normalization), quantification of gene expression and their clustering, development of AI-based models to identify the connection point between epigenetic memory and plant phenotype (Benlioğlu et al., 2024; Yin et al., 2024). Although, epigenetic data appear to be quite complex and variable, ML and DL methods or models have been consolidated and allow these patterns and their connections to be successfully identified in multiple contexts (Gill et al., 2024; Heping et al., 2024). Thanks to these recently achieved advances in AI, we currently possess extensive and highly accurate knowledge of plant epigenetics in the face of stress conditions as well as other non-stressful conditions. The developing low-cost epigenetic sensors for field use will provide practical tools to monitor epigenetic changes in crops under real-world conditions, which could revolutionize precision agriculture and plant breeding efforts. In addition, establishing crop-specific epigenetic databases will enable centralized resources to organize and share the growing volume of epigenetic data in different crops, facilitating comparative analyses and the development of more robust AI models. Furthermore, investigating the transgenerational inheritance of epigenetic memory remains a crucial area for understanding the long-term impact of environmental stresses on plant adaptation and evolution.

In conclusion, our study highlights: (i) the role of epigenetic marks in controlling and fine-regulating plant phenotypes, and the importance of applying AI to process multi-omics data to identify patterns associated with resistance to adverse conditions; and (ii) the potential of applying transgenerational priming to shape epigenetic marks to improve commercial cultivars' abilities to face stress conditions in the field.

GENERATIVE AI USAGE STATEMENT

During the preparation of this work, the authors utilized Gemini AI tool for the purpose of polishing the text, enhancing its fluency and readability and refining the nuances of the language. After using this tool, the authors carefully reviewed and revised the content where necessary, and take full responsibility for the final version of the publication.

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CONFLICTS OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

AUTHOR CONTRIBUTIONS

F.M. conceptualized the project. J.D., D.F., F.M., P.G., M.M.J.B., D.R.A., P.N.M, V.V., and M.F.B. prepared the original draft and participated in review and editing. J.D., D.F., and V.V. created the figures. D.F. and J.D. finalized the submitted version. All authors read and approved the final submitted version.

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REFERENCES

Acera, M.P., Zhou, Y., Zarnack, K., and Eyras, E. (2023). Concepts and methods for transcriptome-wide prediction of chemical messenger RNA modifications with machine learning. Brief. Bioinform. **24:** bbad163.

Agius, D.R., Kapazoglou, A., Avramidou, E., Baranek, M., Carneros, E., Caro, E., Castiglione, S., Cicatelli, A., Radanovic, A., Ebejer, J.P., et al. (2023). Exploring the crop epigenome: A comparison of DNA methylation profiling techniques. Front. Plant Sci. **14:** 1181039.

Akdogan, G., Tufekci, E.D., Uranbey, S., and Unver, T. (2016). miRNA-based drought regulation in wheat. Funct. Integr. Genomics **16:** 221–233.

Ali, M., Sugimoto, K., Ramadan, A., and Arimura, G. (2013). Memory of plant communications for priming anti-herbivore responses. Sci. Rep. **3:** 1872.

Anastasiadi, D., Venney, C.J., Bernatchez, L., and Wellenreuther, M. (2021). Epigenetic inheritance and reproductive mode in plants and animals. Trends. Ecol. Evol. **36:** 1124–1140.

Armstrong, G., Martino, C., Rahman, G., Gonzalez, A., Vázquez-Baeza, Y., Mishne, G., and Knight, R. (2021). Uniform Manifold Approximation and Projection (UMAP) reveals composite patterns and resolves visualization artifacts in microbiome data. mSystems **6:** 10–1128.

Arslan, E., Schulz, J., and Rai, K. (2021). Machine Learning in epigenomics: Insights into cancer biology and medicine. Biochim. Biophys. Acta, Rev. Cancer **1876:** 188588.

Auge, G., Hankofer, V., Groth, M., Antoniou-Kourounioti, R., Ratikainen, I., and Lampei, C. (2023). Plant environmental memory: Implications, mechanisms and opportunities for plant scientists and beyond. AoB Plants **15:** plad032.

Basso, M.F., Ferreira, P.C.G., Kobayashi, A.K., Harmon, F.G., Nepomuceno, A.L., Molinari, H.B.C., and Grossi-de-Sa, M.F. (2019). MicroRNAs and new biotechnological tools for its modulation and improving stress tolerance in plants. Plant Biotechnol. J. **17:** 1482–1500.

Basso, M.F., Neves, M.F., and Grossi-de-Sa, M.F. (2024). Agriculture evolution, sustainability and trends, focusing on Brazilian agribusiness: A review. Front. Sustain. Food Syst. **7:** 1296337.

Basso, M.F., Vásquez, D.D.N., Campos-Pinto, E.R., Pinheiro, D.H., Cruz, B., Maktura, G.C., Guidelli, G.V., Marques-Souza, H., and Grossi-de-Sa, M.F. (2025). Progress and opportunities of *in planta* and topical RNAi for the biotechnological control of agricultural pests. Agronomy **15:** 859.

Baulcombe, D.C., and Dean, C. (2014). Epigenetic regulation in plant responses to the environment. Cold Spring Harbor Persp. Biol. **6:** a019471.

Benlioğlu, B., Demirel, F., Türkoğlu, A., Haliloğlu, K., Özaktan, H., Kujawa, S., Piekutowska, M., Wojciechowski, T., and Niedbała, G. (2024).
Insights into drought tolerance of tetraploid wheat genotypes in the germination stage using machine learning algorithms. Agriculture **14:** 206.

Bentham, A.R., De la Concepcion, J.C., Mukhi, N., Zdrzałek, R., Draeger, M., Gorenkin, D., Hughes, R.K., and Banfield, M.J. (2020). A molecular roadmap to the plant immune system. J. Biol. Chem. **295:** 14916–14935.

Berger, M.M.L., Garcia, V., Lacrampe, N., Rubio, B., Decros, G., Pétriacq, P., Flandin, A., Cassan, C., Hilbert-Masson, G., Colombié, S., et al. (2024). Grapevine cell response to carbon deficiency requires transcriptome and methylome reprogramming. Hortic. Res. **12:** uhae277.

Berger, M.M.L., Stammitti, L., Rubio, B., Carrillo, N., Blancquaert, E., Teyssier, E., and Gallusci, P. (2023). Epigenetic a new lever for Grapevine adaptation to climate changes. OENO One **57:** 265–282.

Betti, F., Ladera-Carmona, M.J., Weits, D.A., Ferri, G., Iacopino, S., Novi, G., Svezia, B., Kunkowska, A.B., Santaniello, A., Piaggesi, A., et al. (2021). Exogenous miRNAs induce post-transcriptional gene silencing in plants. Nat. Plants **7:** 1379–1388.

Bhadouriya, S.L., Mehrotra, S., Basantani, M.K., Loake, G.J., and Mehrotra, R. (2021). Role of chromatin architecture in plant stress responses: An update. Front Plant Sci. **11:** 603380.

Bilichak, A., and Kovalchuk, I. (2016). Transgenerational response to stress in plants and its application for breeding. J. Exp. Bot. **67:** 2081–2092.

Bilichak, A., Ilnytskyy, Y., Wāycicki, R., Kepeshchuk, N., Fogen, D., and Kovalchuk, I. (2015). The elucidation of stress memory inheritance in *Brassica rapa* plants. Front. Plant Sci. **6:** 1–20.

Böhmdorfer, G., Sethuraman, S., Rowley, M.J., Krzyszton, M., Rothi, M.H., Bouzit, L., and Wierzbicki, A.T. (2016). Long non-coding RNA produced by RNA polymerase V determines boundaries of heterochromatin. eLife **5:** e19092.

Boye, C., Nirmalan, S., Ranjbaran, A., and Luca, F. (2024). Genotype × environment interactions in gene regulation and complex traits. Nat. Genet. **56:** 1057–1068.

Breiman, L. (2001). Random Forests. Mach. Learn. **45:** 5–32.

Brieuc, M.S.O., Waters, C.D., Drinan, D.P., and Naish, K.A. (2018). A practical introduction to Random Forest for genetic association studies in ecology and evolution. Mol. Ecol. Resour. **18:** 755–766.

Bröker, F., Holt, L.L., Roads, B.D., Dayan, P., and Love, B.C. (2024). Demystifying unsupervised learning: How it helps and hurts. Trends. Cogn. Sci. **28:** 974–986.

Brzezinka, K., Altmann, S., Czesnick, H., Nicolas, P., Gorka, M., Benke, E., Kabelitz, T., Jähne, F., Graf, A., Kappel, C., et al. (2016). Arabidopsis FORGETTER1 mediates stress-induced chromatin memory through nucleosome remodeling. eLife **5:** 1–23.

Butera, A., Smirnova, L., Ferrando-May, E., Hartung, T., Brunner, T., Leist, M., and Amelio, I. (2023). Deconvoluting gene and environment interactions to develop an "epigenetic score meter" of disease. EMBO Mol. Med. **15:** e18208.

Cai, J., Shen, L., Kang, H., and Xu, T. (2025). RNA modifications in plant adaptation to abiotic stresses. Plant Commun. **6:** 2101229.

Cai, L., Gao, M., Ren, X., Fu, X., Xu, J., Wang, P., and Chen, Y. (2022). MILNP: Plant lncRNA–miRNA interaction prediction based on improved linear neighborhood similarity and label propagation. Front. Plant Sci. **13:** 861886.

Cai, Q., Qiao, L., Wang, M., He, B., Lin, F.M., Palmquist, J., Huang, S.D., and Jin, H. (2018). Plants send small RNAs in extracellular vesicles to fungal pathogen to silence virulence genes. Science **360:** 1126–1129.

Calvo, P., Gagliano, M., Souza, G.M., and Trewavas, A. (2020). Plants are intelligent, here's how. Ann. Bot. **125:** 11–28.

Cambiagno, D.A., Nota, F., Zavallo, D., Rius, S., Casati, P., Asurmendi, S., and Alvarez, M.E. (2018). Immune receptor genes and pericentromeric transposons as targets of common epigenetic regulatory elements. Plant J. **96:** 1178–1190.

Cao, W., Gan, L., Wang, C., Zhao, X., Zhang, M., Du, J., Zhou, S., and Zhu, C. (2021). Genome-wide identification and characterization of potato long non-coding RNAs associated with *Phytophthora infestans* resistance. Front. Plant Sci. **12:** 619062.

Catoni, M., Alvarez-Venegas, R., Worrall, D., Holroyd, G., Barraza, A., Luna, E., Ton, J., and Roberts, M.R. (2022). Long-lasting defence priming by baminobutyric acid in tomato is marked by genome-wide changes in DNA methylation. Front. Plant Sci. **13:** 1–13.

Cembrowska-Lech, D., Krzemińska, A., Miller, T., Nowakowska, A., Adamski, C., Radaczyńska, M., Mikiciuk, G., and Mikiciuk, M. (2023). An integrated multi-omics and artificial intelligence framework for advance plant phenotyping in horticulture. Biology **12:** 1298.

Champigny, M.J., Unda, F., Skyba, O., Soolanayakanahally, R.Y., Mansfield, S.D., and Campbell, M.M. (2020). Learning from methylomes: Epigenomic correlates of *Populus balsamifera* traits based on deep learning models of natural DNA methylation. Plant Biotechnol. J. **18:** 1361–1375.

Chang, H., Zhang, H., Zhang, T., Su, L., Qin, Q.M., Li, G., Li, X., Wang, L., Zhao, T., Zhao, E., et al. (2022). A multi-level iterative bi-clustering method for discovering miRNA co-regulation network of abiotic stress tolerance in soybeans. Front. Plant Sci. **13:** 860791.

Chekanova, J.A. (2015). Long non-coding RNAs and their functions in plants. Curr. Opin. Plant Biol. **27:** 207–216.

Chen, H., Feng, H., Zhang, X., Zhang, C., Wang, T., and Dong, J. (2019a). An Arabidopsis E3 ligase HUB2 increases histone H2B monoubiquitination and enhances drought tolerance in transgenic cotton. Plant Biotechnol. J. **17:** 556–568.

Chen, J., Paw U, K.T., North, M., and Franklin, J.F. (2024). The contributions of microclimatic information in advancing ecosystem science. Agric. For. Meteorol. **355:** 110105.

Chen, K., Tang, W.-S., Zhou, Y.-B., Xu, Z.-S., Chen, J., Ma, Y.-Z., Chen, M., and Li, H.Y. (2020). Overexpression of *GmUBC9* gene enhances plant drought resistance and affects flowering time via histone H2B monoubiquitination. Front. Plant Sci. **11:** 555794.

Chen, T., and Guestrin, C. (2016). XGBoost: A scalable tree boosting system. In *Proceedings of the 22nd ACM SIGKDDInternational Conference on Knowledge Discovery and Data Mining*. Balaji, K., Mohak, S., eds, (New York: Association for Computing Machinery), pp. 785–794.

Chen, X., and Ishwaran, H. (2012). Random forests for genomic data analysis. Genomics **99:** 323–329.

Chen, X., Sun, Y.Z., Guan, N.N., Qu, J., Huang, Z.A., Zhu, Z.X., and Li, J.Q. (2019b). Computational models for lncRNA function prediction and functional similarity calculation. Brief Funct. Genomics **18:** 58–82.

Crisp, P.A., Ganguly, D., Eichten, S.R., Borevitz, J.O., and Pogson, B.J. (2016). Reconsidering plant memory: Intersections between stress recovery, RNA turnover, and epigenetics. Sci. Adv. **2:** e1501340.

Cui, X., Liang, Z., Shen, L., Zhang, Q., Bao, S., Geng, Y., Zhang, B., Leo, V., Vardy, L.A., Lu, T., et al. (2017). 5-methylcytosine RNA methylation in *Arabidopsis thaliana*. Mol. Plant **10:** 1387–1399.

Dai, W., Zhu, W., Zhou, G., Liu, G., Xu, J., Zhou, H., Hu, Y., Liu, Z., Li, J., and Li, L. (2024). AISOA-SSformer: An effective image segmentation method for rice leaf disease based on the Transformer architecture. Plant Phenomics **6:** 0218.

De-La-Peña, C., Rangel-Cano, A., and Alvarez-Venegas, R. (2012). Regulation of disease-responsive genes mediated by epigenetic factors: Interaction of *Arabidopsis-Pseudomonas*. Mol. Plant Pathol. **13:** 388–398.

Devesa-Guerra, I., Morales-Ruiz, T., Pérez-Roldán, J., Parrilla-Doblas, J.T., Dorado-León, M., García-Ortiz, M.V., Ariza, R.R., and Roldán-Arjona, T. (2020). DNA methylation editing by CRISPR-guided excision of 5-methylcytosine. J. Mol. Biol. **432:** 2204–2216.

Dobránszki, J., Agius, D.R., Berger, M.M.J., Moschou, P.N., Gallusci, P., and Martinelli, F. (2025). Plant memory and communication of encounters. Trends Plant Sci. **30:** 199–212.

Donald, C.M. (1968). The breeding of crop ideotypes. Euphytica **17:** 385–403.

Du, H., Wang, J., Hui, J., Zhang, L., and Wang, H. (2024). DenseGNN: Universal and scalable deeper graph neural networks for high-performance property prediction in crystals and molecules. Npj Comput. Mater. **10:** 292.

Dubey, A., Lee, J., Kwon, S., Lee, Y.H., and Jeon, J. (2019). A MYST family histone acetyltransferase, MoSAS3, is required for development and pathogenicity in the rice blast fungus. Mol. Plant Pathol. **20:** 1491–1505.

Duran-Flores, D., and Heil, M. (2018). Extracellular self-DNA as a damage-associated molecular pattern (DAMP) that triggers self-specific immunity induction in plants. Brain Behav. Immun. **72:** 78–88.

Farkas, D., and Dobránszki, J. (2024). Vegetal memory through the lens of transcriptomic changes—Recent progress and future practical prospects for exploiting plant transcriptional memory. Plant Signal. Behav. **19:** 2383515.

Ferdous, J., Hussain, S.S., and Shi, B.J. (2015). Role of micro RNAs in plant drought tolerance. Plant Biotechnol. J. **13:** 293–305.

Fernández, M., and Miranda-Saavedra, D. (2012). Genome-wide enhancer prediction from epigenetic signatures using genetic algorithm-optimized support vector machines. Nucl. Acids Res. **40:** e77.

Friedrich, T., Faivre, L., Bäurle, I., and Schubert, D. (2019). Chromatin-based mechanisms of temperature memory in plants. Plant, Cell Environ. **42:** 762–770.

Furci, L., Jain, R., Stassen, J., Berkowitz, O., Whelan, J., Roquis, D., Baillet, V., Colot, V., Johannes, F., and Ton, J. (2019). Identification and characterisation of hypomethylated DNA loci controlling quantitative resistance in Arabidopsis. eLife **8:** e40655.

Gallusci, P., Agius, D.R., Moschou, P.N., Dobránszki, J., Kaiserli, E., and Martinelli, F. (2023). Deep inside the epigenetic memories of stressed plants. Trends Plant Sci. **28:** 142–153.

Gallusci, P., Dai, Z., Génard, M., Gauffretau, A., Leblanc-Fournier, N., Richard-Molard, C., Vile, D., and Brunel-Muguet, S. (2017). Epigenetics for plant improvement: Current knowledge and modeling avenues. Trends Plant Sci. **22:** 610–623.

Galviz, Y., Souza, G.M., and Lüttge, U. (2022). The biological concept of stress revisited: Relations of stress and memory of plants as a matter of space-time. Theor. Exp. Plant Physiol. **34:** 239–264.

Gamarnik, D. (2023). Barriers for the performance of graph neural networks (GNN) in discrete random structures. Proc. Natl. Acad. Sci. U.S.A. **120:** e2314092120.

Ganguly, D.R., Crisp, P.A., Eichten, S.R., and Pogson, B.J. (2017). The Arabidopsis DNA methylome is stable under transgenerational drought stress. Plant Physiol. **175:** 1893–1912.

Ganie, S.A., McMulkin, N., and Devoto, A. (2024). The role of priming and memory in rice environmental stress adaptation: Current knowledge and perspectives. Plant Cell Environ. **47:** 1895–1915.

Gao, Z., Liu, Q., Zeng, W., Jiang, R., and Wong, W.H. (2024). EpiGePT: A pretrained transformer-based language model for context-specific human epigenomics. Genome Biol. **25:** 310.

Gayacharan, and Joel, A.J. (2013). Epigenetic responses to drought stress in rice (*Oryza sativa* L.). Physiol. Mol. Biol. Plants **19:** 379–387.

Georgieva, M., and Vassileva, V. (2023). Stress management in plants: Examining provisional and unique dose-dependent responses. Int. J. Mol. Sci. **24:** 5105.

Ghahramani, A., Watt, F.M., and Luscombe, N.M. (2018). Generative adversarial networks simulate gene expression and predict perturbations in single cells. BioRxiv. https://doi.org/10.1101/262501

Gill, S.S., Khan, N.A., Agarwala, N., Singh, K., Sunkar, R., and Tuteja, N. (2024). ncRNAs in plant development and stress responses. Plant Physiol. Biochem. **214:** 108950.

Gill, T., Gill, S.K., Saini, D.K., Chopra, Y., de Koff, J.P., and Sandhu, K.S. (2022). A comprehensive review of high throughput phenotyping and machine learning for plant stress phenotyping. Phenomics **2:** 156–183.

Greaves, I.K., Groszmann, M., Wang, A., Peacock, W.J., and Dennis, E.S. (2014). Inheritance of trans chromosomal methylation patterns from Arabidopsis F1 hybrids. Proc. Natl. Acad. Sci. U.S.A. **111**: 2017–2022

Guarino, F., Cicatelli, A., Castiglione, S., Agius, D.R., Orhun, G.E., Fragkostefanakis, S., Leclercq, J., Dobránszki, J., Kaiserli, E., Lieberman-Lazarovich, M., et al. (2022). An epigenetic alphabet of crop adaptation to climate change. Front. Genet. **13:** 818727.

Guarino, F., Cicatelli, A., Nissim, W.G., Colzi, I., Gonnelli, C., Basso, M.F., Vergata, C., Contaldi, F., Martinelli, F., and Castiglione, S. (2024). Epigenetic changes induced by chronic and acute chromium stress treatments in *Arabidopsis thaliana* identified by the MSAP-Seq. Chemosphere **362:** 142642.

Guindon, B., and Zhang, Y. (2017). Application of the dice coefficient to accuracy assessment of object-based image classification. Can. J. Remote Sens. **43:** 48–61.

Guo, C., Ma, X., Gao, F., and Guo, Y. (2023b). Off-target effects in CRISPR/Cas9 gene editing. Front. Bioeng. Biotechnol. **11:** 1143157.

Guo, Y., Tan, Y., Qu, M., Hong, K., Zeng, L., Wang, L., Zhuang, C., Qian, Q., Hu, J., and Xiong, G. (2023a). OsWR2 recruits HDA704 to regulate the deacetylation of H4K8ac in the promoter of OsABI5 in response to drought stress. J. Integr. Plant Biol. **65:** 1651–1669.

Halter, T., Wang, J., Amesefe, D., Lastrucci, E., Charvin, M., Singla Rastogi, M., and Navarro, L. (2021). The Arabidopsis active demethylase ROS1 *cis*-regulates defence genes by erasing DNA methylation at promoter-regulatory regions. eLife **10:** e62994.

Han, R., Shoaib, Y., Cai, J., and Kang, H. (2023). ALKBH10B-mediated 6mA demethylation is crucial for drought tolerance by affecting mRNA stability in Arabidopsis. Environ. Exp. Bot. **209:** 105306.

Harris, C.J., Amtmann, A., and Ton, J. (2023). Epigenetic processes in plant stress priming: Open questions and new approaches. Curr. Opin. Plant Biol. **75:** 102432.

Hasan, M., Nishat, Z.S., Hasan, M.S., Hossain, T., and Ghosh, A. (2024). Identification of 6mA RNA methylation genes in *Oryza sativa* and expression profiling in response to different developmental and environmental stimuli. Biochem. Biophys. Rep. **38:** 101677.

Hemenway, E.A., and Gehring, M. (2023). Epigenetic regulation during plant development and the capacity for epigenetic memory. Ann. Rev. Plant Biol. **74:** 87–109.

Heping, W., Lan, C., Ping, W., Hanbing, H., Rui, G., Jingdong, C., Huixia, Z., Changli, Z., and Xiaoyun, L. (2024). Genome-wide

mapping of main histone modifications and coordination regulation of metabolic genes under salt stress in pea (*Pisum sativum* L). Hortic. Res. **11:** uhae259.

Hilker, M., and Schmülling, T. (2019). Stress priming, memory, and signalling in plants. Plant Cell Environ. **42:** 753–761.

Hinton, G.E., Osindero, S., and Teh, Y.W. (2006). A fast learning algorithm for deep belief nets. Neural Comput. **18:** 1527–1554.

Hosmer, D.W., Jr., Lemeshow, S., and Sturdivant, R.X. (2013). Exact methods for logistic regression models. In *Applied Logistic Regression*, Hosmer, D.W., Lemeshow, S., eds, (New Jersey: John Wiley & Sons), pp. 387–394.

Hou, Y., Wang, L., Wang, L., Liu, L., Li, L., Sun, L., Rao, Q., Zhang, J., and Huang, S. (2015). JMJ704 positively regulates rice defense response against *Xanthomonas oryzae* pv. *oryzae* infection via reducing H3K4me2/3 associated with negative disease resistance regulators. BMC Plant Biol. **15:** 286.

Hu, J., Cai, J., Xu, T., and Kang, H. (2022). Epitranscriptomic mRNA modifications governing plant stress responses: Underlying mechanism and potential application. Plant Biotechnol. J. **20:** 2245–2257.

Huang, C.Y., and Jin, H. (2022). Coordinated epigenetic regulation in plants: A potent managerial tool to conquer biotic stress. Front. Plant Sci. **12:** 795274.

Huang, K., Tian, J., Sun, L., Hu, H., Huang, X., Zhou, S., Deng, A., Zhou, Z., Jiang, M., Li, G., et al. (2025). TransGeneSelector: Using a transformer approach to mine key genes from small transcriptomic datasets in plant responses to various environments. BMC Genomics **26:** 259.

Ibragić, S., Dahija, S., and Karalija, E. (2025). The good, the bad, and the epigenetic: Stress-induced metabolite regulation and transgenerational effects. Epigenomes **9:** 10.

Iqbal, Z., Iqbal, M.S., Hashem, A., Abd Allah, E.F., and Ansari, M.I. (2021). Plant defense responses to biotic stress and its interplay with fluctuating dark/light conditions. Front. Plant Sci. **12:** 631810.

Jahedi, A., Salehi, M., Goltapeh, E.M., and Safaie, N. (2023). Multilayer perceptron-genetic algorithm as a promising tool for modeling cultivation substrate of *Auricularia cornea* Native to Iran. PLoS ONE **18:** e0281982.

Jaskiewicz, M., Conrath, U., and Peterhälnsel, C. (2011). Chromatin modification acts as a memory for systemic acquired resistance in the plant stress response. EMBO Rep. **12:** 50–55.

Javed, A., Rizzo, D.M., Lee, B.S., and Gramling, R. (2024). Sometimes: Self organizing maps for time series clustering and its application to serious illness conversations. Data Min. Knowl. Discov. **38:** 813–839.

Jiang, W., Han, H., Zhang, Y., Wang, J.a, He, M., Gu, W., Mu, J., and Cheng, X. (2024). Graph neural networks for routing optimization: Challenges and opportunities. Sustainability **16:** 9239.

Kambona, C.M., Koua, P.A., Léon, J., and Ballvora, A. (2023). Stress memory and its regulation in plants experiencing recurrent drought conditions. Theor. Appl. Genet. **136:** 26.

Kang, M., Ko, E., and Mersha, T.B. (2022). A roadmap for multi-omics data integration using deep learning. Brief. Bioinform. **23:** bbab454.

Kasai, A., Bai, S., Hojo, H., and Harada, T. (2016). Epigenome editing of potato by grafting using transgenic tobacco as siRNA donor. PLoS ONE **11:** e0161729.

Kim, D.H., and Rossi, J.J. (2008). RNAi mechanisms and applications. Biotechniques **44:** 613–616.

Kim, J.H. (2021). Multifaceted chromatin structure and transcription changes in plant stress response. Int. J. Mol. Sci. **22:** 2013.

Kim, Y., Barnaby, J.Y., and Warnke, S.E. (2024). Development of a low-cost automated greenhouse imaging system with machine learning-based processing for evaluating genetic performance of drought tolerance in a bentgrass hybrid population. Comput. Electr. Agric. **224:** 108896.

Kimotho, R.N., and Maina, S. (2024). Unraveling plant-microbe interactions: Can integrated omics approaches offer concrete answers. J. Exp. Bot. **75:** 1289–1313.

Kinoshita, T., and Seki, M. (2014). Epigenetic memory for stress response and adaptation in plants. Plant Cell Physiol. **55:** 1859–1863.

Konermann, S., Brigham, M.D., Trevino, A.E., Joung, J., Abudayyeh, O.O., Barcena, C., Hsu, P.D., Habib, N., Gootenberg, J.S., Nishimasu, H., et al. (2015). Genome-scale transcriptional activation by an engineered CRISPR-Cas9 complex. Nature **517:** 583–588.

Koo, P.K., and Eddy, S.R. (2019). Representation learning of genomic sequence motifs with convolutional neural networks. PLoS Comput. Biol. **15:** e1007560.

Koornneef, A., and Pieterse, C.M.J. (2008). Cross talk in defense signaling. Plant Physiol. **146:** 839–844.

Kumar Meher, P., Hati, S., Sahu, T.K., Pradhan, U., Gupta, A., and Rath, S.N. (2022). SVM-Root: Identification of root-associated proteins in plants by employing the Support Vector Machine with sequence-derived features. Curr. Bioinform. **19:** 91–102.

Kutashev, K., and Moschou, P.N. (2025). The role of membrane-biomolecular condensate interactions in stress. Plant Stress **16:** 100810.

Kuznicki, D., Meller, B., Arasimowicz-Jelonek, M., Braszewska-Zalewska, A., Drozda, A., and Floryszak-Wieczorek, J. (2019). BABA-induced DNA methylome adjustment to intergenerational defense priming in potato to *Phytophthora infestans*. Front. Plant Sci. **10:** 650.

Lam, H.Y.I., Ong, X.E., and Mutwil, M. (2024). Large language models in plant biology. Trends Plant Sci. **29:** 1145–1155.

Lämke, J., and Bäurle, I. (2017). Epigenetic and chromatin-based mechanisms in environmental stress adaptation and stress memory in plants. Genome Biol. **18:** 124.

LeCun, Y., Bengio, Y.and Hinton, G. (2015). Deep learning. Nature **521:** 436–444.

Le Gac, A.L., Lafon-Placette, C., Chauveau, D., Segura, V., Delaunay, A., Fichot, R., Marron, N., Le Jan, I., Berthelot, A., Bodineau, G., et al. (2018). Winter-dormant shoot apical meristem in poplar trees shows environmental epigenetic memory. J. Exp. Bot. **69:** 4821–4837.

Li, C., Xu, M., Cai, X., Han, Z., Si, J., and Chen, D. (2022a). Jasmonate signaling pathway modulates plant defense, growth, and their trade-offs. Int. J. Mol. Sci. **23:** 3945.

Li, K., Yao, S., Zhang, Z., Cao, B., Wilson, C.M., Kalos, D., Kuan, P.F., Zhu, R., and Wang, X. (2022b). Efficient gradient boosting for prognostic biomarker discovery. Bioinformatics **38:** 1631–1638.

Li, Y., Quan, L., Zhou, Y., Jiang, Y., Li, K., Wu, T., and Lyu, Q. (2022c). Identifying modifications on DNA-bound histones with joint deep learning of multiple binding sites in DNA sequence. Bioinformatics **38:** 4070–4077.

Li, Y., Yin, M., Wang, J., Zhao, X., Xu, J., Wang, W., and Fu, B. (2025a). Epitranscriptome profiles reveal participation of the RNA methyltransferase gene *OsMTA1* in rice seed germination and salt stress response. BMC Plant Biol. **25:** 115.

Li, Z., Hu, Y., Chang, M., Kashif, M.H., Tang, M., Luo, D., Cao, S., Lu, H., Zhang, W., Huang, Z., et al. (2021). 5-Azacytidine pre-treatment alters DNA methylation levels and induces genes responsive to salt stress in kenaf (*Hibiscus cannabinus* L.). Chemosphere **271:** 129562.

Li, Z.P., Du, Z., Huang, D.S., and Teschendorff, A.E. (2025b). Interpretable deep learning of single-cell and epigenetic data reveals novel molecular insights in aging. Sci. Rep. **15:** 5048.

Liang, M.-H., and Jiang, J.-G. (2021). Two DNA methyltransferase inhibitors (5-azacytidine and zebularine) affected the carotenoid accumulation in two green algae, *Chlamydomonas reinhardtii* and *Dunaliella bardawil*. In *The 8th International Horticulture Research Conference*. Chen F., van Nocker, S., eds, (Nanjing: Nanjing Agricultural University), pp. 1–4.

Liang, Z., Riaz, A., Chachar, S., Ding, Y., Du, H., and Gu, X. (2020). Epigenetic modifications of mRNA and DNA in plants. Mol. Plant **13:** 14–30.

Linderman, G.C., and Steinerberger, S. (2019). Clustering with t-SNE, provably. SIAM J. Math. Data Sci. **1:** 313–332.

Liu, C., Mentzelopoulou, A., Hatzianestis, I.H., Tzagkarakis, E., Skaltsogiannis, V., Ma, X., Michalopoulou, V.A., Romero-Campero, F.J., Romero-Losada, A.B., Sarris, P.F., et al. (2024). A proxitome-RNA-capture approach reveals that processing bodies repress coregulated hub genes. Plant Cell **36:** 559–584.

Liu, H., Able, A.J., and Able, J.A. (2022). Priming crops for the future: Rewiring stress memory. Trends Plant Sci. **27:** 699–716.

Liu, H., Begik, O., and Novoa, E.M. (2021b). EpiNano: Detection of m(6)A RNA modifications using Oxford Nanopore direct RNA sequencing. Methods Mol. Biol. **2298:** 31–52.

Liu, J., Feng, L., Gu, X., Deng, X., Qiu, Q., Li, Q., Zhang, Y., Wang, M., Deng, Y., Wang, E., et al. (2019a). An H3K27me3 demethylase-HSFA2 regulatory loop orchestrates transgenerational thermomemory in Arabidopsis. Cell Res. **29:** 379–390.

Liu, S., Bao, Y., Deng, H., Liu, G., Han, Y., Wu, Y., Zhang, T., and Chen, C. (2021a). The methylation inhibitor 5-aza-2′-deoxycytidine induces genome-wide hypomethylation in rice. Preprint (Version 1) available at Research Square. **15:** 35.

Liu, Y., Wang, D., He, F., Wang, J., Joshi, T., and Xu, D. (2019b). Phenotype prediction and genome-wide association study using deep convolutional neural network of soybean. Front. Genet. **10:** 1091.

Long, N., Gianola, D., Rosa, G.J., and Weigel, K.A. (2011). Application of support vector regression to genome-assisted prediction of quantitative traits. Theor. Appl. Genet. **123:** 1065–1074.

López, M.E., Denoyes, B., and Bucher, E. (2024). Epigenomic and transcriptomic persistence of heat stress memory in strawberry (*Fragaria vesca*). BMC Plant Biol. **24:** 405.

López Sánchez, A., Stassen, J.H., Furci, L., Smith, L.M., and Ton, J. (2016). The role of DNA (de)methylation in immune responsiveness of Arabidopsis. Plant J. **88:** 361–374.

Luna, E., López, A., Kooiman, J., and Ton, J. (2014). Role of NPR1 and KYP in long-lasting induced resistance by β-aminobutyric acid. Front. Plant Sci. **5:** 1–8.

Luo, C., Bashir, N.H., Li, Z., Liu, C., Shi, Y., and Chu, H. (2024). Plant microRNAs regulate the defense response against pathogens. Front. Microbiol. **15:** 1434798.

Luo, Q., Zeng, W., Chen, M., Peng, G., Yuan, X., and Yin, Q. (2023). Self-Attention and Transformers: Driving the evolution of large language models. In *6th International Conference on Electronic Information and Communication Technology (ICEICT)*, ed: unknown, (Qingdao: IEE), pp. 401–405.

Luo, Y., and Yang, Z. (2024). DynGAN: Solving mode collapse in GANs with dynamic clustering. IEEE. Trans. Pattern. Anal. Mach. Intell. **46:** 5493–5503.

Ma, S., and Dai, Y. (2011). Principal component analysis based methods in bioinformatics studies. Brief. Bioinform. **12:** 714–722.

Ma, S., Tang, N., Li, X., Xie, Y., Xiang, D., Fu, J., Shen, J., Yang, J., Tu, H., Li, X., et al. (2019). Reversible histone H2B monoubiquitination fine-tunes abscisic acid signaling and drought response in rice. Mol. Plant **12:** 263–277.

Maleki, N., Ghorbani, A., Rostami, M., and Maina, S. (2025). Elucidating long non-coding RNA networks in tomato plants in response to *Funneliformis mosseae* colonization and cucumber mosaic virus infection. BMC Plant Biol. **25:** 495.

Mansoor, S., Karunathilake, E.M., Tuan, T.T., and Chung, Y.S. (2024). Genomics, phenomics, and machine learning in transforming plant research: Advancements and challenges. Hortic. Plant J. **11:** 486–503.

Marzec, M. (2022). MicroRNA: A new signal in plant-to-plant communication. Trends Plant Sci. **27:** 418–419.

Mathur, K., Gupta, A., Rawat, V., Sharma, V., and Shakya, S. (2024). Role of noncoding RNAs in host-pathogen interactions: A systems biology approach. In *Systems Biology Approaches for Host-Pathogen Interaction Analysis*, Ashraf, M.T., Khan, A.A., Aldakheel, F.M., eds. (Academic Press), pp. 213–249.

Mavaie, P., Holder, L., Beck, D., and Skinner, M.K. (2021). Predicting environmentally responsive transgenerational differential DNA methylated regions (epimutations) in the genome using a hybrid deep-machine learning approach. BMC Bioinformatics **22:** 1–25.

Meller, B., Kuznicki, D., Arasimowicz-Jelonek, M., Deckert, J., and Floryszak-Wieczorek, J. (2018). BABA-primed histone modifications in potato for intergenerational resistance to *Phytophthora infestans*. Front. Plant Sci. **9:** 1228.

Mienye, I.D., and Swart, T.G. (2024). A comprehensive review of Deep Learning: Architectures, recent advances, and applications. Information **15:** 755.

Mienye, I.D., Swart, T.G., and Obaido, G. (2024). Recurrent neural networks: A comprehensive review of architectures, variants, and applications. Information **15:** 517.

Mierziak, J., and Wojtasik, W. (2024). Epigenetic weapons of plants against fungal pathogens. BMC Plant Biol. **24:** 175.

Miglani, G.S., and Kaur, M. (2025). Multi-epiomics and crop improvement for sustainable agriculture. In *Omics and Genome Editing: Revolution in Crop Improvement for Sustainable Agriculture*, Sharma, K., ed, (Cham: Springer Nature), pp. 37–53.

Miryeganeh, M. (2025). Epigenetic mechanisms driving adaptation in tropical and subtropical plants: Insights and future directions. Plant Cell Environ. **48:** 3487–3499.

Mishra, S., Roychowdhury, R., Ray, S., Hada, A., Kumar, A., Sarker, U., Aftab, T., and Das, R. (2024). Salicylic acid (SA)-mediated plant immunity against biotic stresses: An insight on molecular components and signaling mechanism. Plant Stress **11:** 100427.

Molinier, J., Ries, G., Zipfel, C., and Hohn, B. (2006). Transgeneration memory of stress in plants. Nature **442:** 1046–1049.

Molnar, A., Melnyk, C., and Baulcombe, D.C. (2011). Silencing signals in plants: A long journey for small RNAs. Genome Biol. **12:** 215.

Moore, B.M., Wang, P., Fan, P., Lee, A., Leong, B., Lou, Y.R., Schenck, C.A., Sugimoto, K., Last, R., Lehti-Shiu, M.D., et al. (2020). Within- and cross-species predictions of plant specialized metabolism genes using transfer learning. isP **2**: diaa005.

Murmu, S., Sinha, D., Chaurasia, H., Sharma, S., Das, R., Jha, G.K., and Archak, S. (2024). A review of artificial intelligence-assisted omics techniques in plant defense: Current trends and future directions. Front. Plant Sci. **15:** 1292054.

N'Diaye, A., Byrns, B., Cory, A.T., Nilsen, K.T., Walkowiak, S., Sharpe, A., Robinson, S.J., and Pozniak, C.J. (2020). Machine learning analyses of methylation profiles uncovers tissue-specific gene expression patterns in wheat. Plant Genome **13:** e20027.

Nejat, N., and Mantri, N. (2018). Emerging roles of long non-coding RNAs in plant response to biotic and abiotic stresses. Crit. Rev. Biotechnol. **38:** 93–105.

Nikkilä, J., Törönen, P., Kaski, S., Venna, J., Castrén, E., and Wong, G. (2002). Analysis and visualization of gene expression data using self-organizing maps. Neural Netw. **15:** 953–966.

Nisha, K., Augustine, C., Anand, A.J., and Kamesh, M. (2024). Deep learning in smart agriculture. In *Advanced Technologies for Smart Agriculture*. Kalaiselvi, K.A., Anand, J.A., Tanwar, P., Raza, H., eds, (New York: River Publishers), pp. 153–175.

Nobori, T., Monell, A., Lee, T.A., Sakata, Y., Shirahama, S., Zhou, J., Nery, J.R., Mine, A., and Ecker, J.R. (2025). A rare PRIMER cell state in plant immunity. Nature **638:** 197–205.

Ogneva, Z.V., Suprun, A.R., Dubrovina, A.S., and Kiselev, K.V. (2019). Effect of 5-azacytidine induced DNA demethylation on abiotic stress tolerance in *Arabidopsis thaliana*. Plant Protect. Sci **55:** 73–80.

Oladayo Esan, D.O., Adewale Owolawi, P., and Tu, C. (2023). Generative adversarial networks: Applications, challenges, and open issues. In *Deep Learning—Recent Findings and Research*, Domínguez-Morales, M.J., Civit-Masot, J., Muñoz-Saavedra, L., Damaševičius, R., eds, (Rijeka: IntechOpen), pp. 1–25.

Olive, D.J. (ed) (2017). *Linear Regression*. Springer, Cham.

Omony, J., Nussbaumer, T., and Gutzat, R. (2020). DNA methylation analysis in plants: Review of computational tools and future perspectives. Brief. Bioinform. **21:** 906–918.

Onosatu, H., Fujimoto, G., Higami, T., Sakamoto, T., Yamada, A., Suzuki, T., Ozawa, R., Matsunaga, S., Seki, M., Ueda, M., et al. (2022). Sustained defense response via volatile signaling and its epigenetic transcriptional regulation. Plant Physiol. **189:** 922–933.

Osakabe, A., Takizawa, Y., Horikoshi, N., Hatazawa, S., Negishi, L., Sato, S., Berger, F., Kakutani, T., and Kurumizaka, H. (2024). Molecular and structural basis of the chromatin remodeling activity by Arabidopsis DDM1. Nat. Commun. **15:** 5187.

Padhiary, M., Saha, D., Kumar, R., Sethi, L.N., and Kumar, A. (2024). Enhancing precision agriculture: A comprehensive review of machine learning and AI vision applications in all-terrain vehicle for farm automation. Smart Agr. Technol. **8:** 100483.

Pan, Y., Jia, Y., Liu, W., Zhao, Q., Pan, W., Jia, Y., Lv, S., Liu, X., and Nie, X. (2024). Transcriptome-wide 6mA methylation profile reveals its potential role underlying drought response in wheat (*Triticum aestivum* L.). Planta **260:** 65.

Papareddy, R.K., Páldi, K., Paulraj, S., Kao, P., Lutzmayer, S., and Nodine, M.D. (2020). Chromatin regulates expression of small RNAs to help maintain transposon methylome homeostasis in Arabidopsis. Genome Biol. **21:** 1–24.

Papikian, A., Liu, W., Gallego-Bartolomé, J., and Jacobsen, S.E. (2019). Site-specific manipulation of Arabidopsis loci using CRISPR-Cas9 SunTag systems. Nat. Commun. **10:** 729.

Pardal, A.J., Piquerez, S.J., Dominguez-Ferreras, A., Frungillo, L., Mastorakis, E., Reilly, E., Latrasse, D., Concia, L., Gimenez-Ibanez, S., Spoel, S.H., et al. (2021). Immunity onset alters plant chromatin and utilizes EDA16 to regulate oxidative homeostasis. PLoS Pathog. **17:** e1009572.

Pasala, R., and Pandey, B.B. (2020). Plant phenomics: High-throughput technology for accelerating genomics. J. Biosci. **45:** 111.

Pastor, V., Luna, E., Mauch-Mani, B., Ton, J., and Flors, V. (2013). Primed plants do not forget. Envi. Exp. Bot. **94:** 46–56.

Patel, J., Chandel, S.T., and Sonker, A. (2024). An optimization driven deep belief network model for crop yield prediction in IoT based smart agriculture. Multim. Tools Appl. **4:** 1–23.

Patwardhan, N., Marrone, S., and Sansone, C. (2023). Transformers in the real world: A survey on NLP applications. Information **14:** 242.

Peng, S., and Rajjou, L. (2024). Advancing plant biology through deep learning-powered natural language processing. Plant Cell Rep. **43:** 208.

Penninckx, I.A., Eggermont, K., Terras, F.R., Thomma, B.P., De Samblanx, G.W., Buchala, A., Métraux, J.P., Manners, J.M., and Broekaert, W.F. (1996). Pathogen-induced systemic activation of a plant defensin gene in Arabidopsis follows a salicylic acid-independent pathway. Plant Cell **8:** 2309–2323.

Piecyk, R.S., Schlegel, L., and Johannes, F. (2022). Predicting 3D chromatin interactions from DNA sequence using Deep Learning. Comput. Struct. Biotechnol. J. **20:** 3439–3448.

Powadi, A., Jubery, T.Z., Tross, M.C., Schnable, J.C., and Ganapathysubramanian, B. (2024). Disentangling genotype and environment specific latent features for improved trait prediction using a compositional autoencoder. Front. Plant Sci. **15:** 1476070.

Po-Wen, C., Singh, P., and Zimmerli, L. (2013). Priming of the Arabidopsis pattern-triggered immunity response upon infection by necrotrophic *Pectobacterium carotovorum* bacteria. Mol. Plant Pathol. **14:** 58–70.

Pradhan, U.K., Meher, P.K., Naha, S., Rao, A.R., and Gupta, A. (2023a). ASLncR: A novel computational tool for prediction of abiotic stress-responsive long non-coding RNAs in plants. Funct. Integr. Genomics **23:** 113.

Pradhan, U.K., Meher, P.K., Naha, S., Rao, A.R., Kumar, U., Pal, S., and Gupta, A. (2023b). ASmiR: A machine learning framework for prediction of abiotic stress-specific miRNAs in plants. Funct. Integr. Genomics **23:** 92.

Prall, W., Sheikh, A.H., Bazin, J., Bigeard, J., Almeida-Trapp, M., Crespi, M., Hirt, H., and Gregory, B.D. (2023). Pathogen-induced m6A dynamics affect plant immunity. Plant Cell **35:** 4155–4172.

Qamar, T., and Bawany, N.Z. (2023). Understanding the black-box: Towards interpretable and reliable deep learning models. PeerJ Comput. Sci. **9:** e1629.

Qi, Q., Hu, B., Jiang, W., Wang, Y., Yan, J., Ma, F., Guan, Q., and Xu, J. (2023). Advances in plant epigenome editing research and its application in plants. Int. J. Mol. Sci. **24:** 3442.

Qin, Y.-M., Tu, Y.-H., Li, T., Ni, Y., Wang, R.-F., and Wang, H. (2025). Deep Learning for sustainable agriculture: A systematic review on applications in lettuce cultivation. Sustainability **17:** 3190.

Quadrana, L., and Colot, V. (2016). Plant transgenerational epigenetics. Annu. Rev. Gen. **50:** 467–491.

Rahman, C.R., Amin, R., Shatabda, S., and Toaha, M.S.I. (2021). A convolution based computational approach towards DNA N6-methyladenine site identification and motif extraction in rice genome. Sci. Rep. UK **11:** 10357.

Ramirez-Prado, J.S., Abulfaraj, A.A., Rayapuram, N., Benhamed, M., and Hirt, H. (2018). Plant immunity: From signaling to epigenetic control of defense. Trends Plant Sci. **23:** 833–844.

Rashedi, K.A., Ismail, M.T., Al Wadi, S., Serroukh, A., Alshammari, T.S., and Jaber, J.J. (2024). Multi-layer perceptron-based classification with application to outlier detection in Saudi Arabia stock returns. J. Risk. Financial Manag. **17:** 69.

Raza, A., Khare, T., Zhang, X., Rahman, M.dM., Hussain, M., Gill, S.S., Chen, Z.-H., Zhou, M., Hu, Z., and Varshney, R.K. (2025). Novel strategies for designing climate-smart crops to ensure sustainable agriculture and future food security. J. Sustain. Agr. Environ. **4:** e70048.

Rendina González, A.P., Preite, V., Verhoeven, K.J.F., and Latzel, V. (2018). Transgenerational effects and epigenetic memory in the clonal plant *Trifolium repens*. Front. Plant Sci. **9:** 1677.

Richards, C.L., Alonso, C., Becker, C., Bossdorf, O., Bucher, E., Colomé-Tatché, M., Durka, W., Engelhardt, J., Gaspar, B., Gogol-Döring, A., et al. (2017). Ecological plant epigenetics: Evidence from model and non-model species, and the way forward. Ecol. Lett. **20:** 1576–1590.

Rico-Chávez, A.K., Franco, J.A., Fernandez-Jaramillo, A.A., Contreras-Medina, L.M., Guevara-González, R.G., and Hernandez-Escobedo, Q. (2022). Machine learning for plant stress modeling: A perspective towards hormesis management. Plants **11:** 970.

Rincón-Riveros, A., Morales, D., Rodríguez, J.A., Villegas, V.E., and López-Kleine, L. (2021). Bioinformatic tools for the analysis and prediction of ncRNA interactions. Int. J. Mol. Sci. **22:** 11397.

Roca Paixão, J.F., Gillet, F.X., Ribeiro, T.P., Bournaud, C., Lourenço-Tessutti, I.T., Noriega, D.D., Melo, B.P.D., de Almeida-Engler, J., and Grossi-de-Sa, M.F. (2019). Improved drought stress tolerance in Arabidopsis by CRISPR/dCas9 fusion with a Histone AcetylTransferase. Sci. Rep. **9:** 8080.

Romero-Rodríguez, B., Petek, M., Jiao, C., Križnik, M., Zagorščak, M., Fei, Z., Bejarano, E.R., Gruden, K., and Castillo, A.G. (2023). Transcriptional and epigenetic changes during tomato yellow leaf curl virus infection in tomato. BMC Plant Biol. **23:** 651.

Roychowdhury, R., Das, S.P., Gupta, A., Parihar, P., Chandrasekhar, K., Sarker, U., Kumar, A., Ramrao, D.P., and Sudhakar, C. (2023).

Multi-omics pipeline and omics-integration approach to decipher plant's abiotic stress tolerance responses. Genes **14:** 1281.

Ruf, L. (2022). Spotlight on plant RNA-containing extracellular vesicles. Curr. Opin. Plant Biol. **69:** 102272.

Sadhukhan, A., Prasad, S.S., Mitra, J., Siddiqui, N., Sahoo, L., Kobayashi, Y., and Koyama, H. (2022). How do plants remember drought? Planta **256:** 7.

Saito, H., Sakata, N., Ishiga, T., and Ishiga, Y. (2022). Efficacy of RNA-spray-induced silencing of Phakopsora pachyrhizi chitin synthase genes to control soybean rust. J. Gen. Plant Pathol. **88:** 203–206.

Salai, B., and Ramapuram, C. (2024). Deep Learning approaches for disease detection based on plant leaf image: A review. In *Intelligent Systems Design and Applications: Deep Learning*, Abraham, A., Bajaj, A., Hanne, T., Hong, T.-P., eds, **2** (Cham: Springer), pp. 323–336.

Sampson, C., Ikenwugwu, T.H., Okagu, I.U., Yahaya, I.I., Odoh, C.K., and Eze, C.N. (2024). Epigenetics: Toward improving crop disease resistance and agronomic characteristics. Plant Biotechnol. Rep. **18:** 1–20.

Sánchez, A.L., Stassen, J.H., Furci, L., Smith, L.M., and Ton, J. (2016). The role of DNA (de) methylation in immune responsiveness of Arabidopsis. Plant J. **88:** 361–374.

Sarkar, S., Ganapathysubramanian, B., Singh, A., Fotouhi, F., Kar, S., Nagasubramanian, K., Chowdhary, G., Das, S.K., Kantor, G., Krishnamurthy, A., et al. (2024). Cyber-agricultural systems for crop breeding and sustainable production. Trends Plant Sci. **29:** 130–149.

Schillheim, B., Jansen, I., Baum, S., Beesley, A., Bolm, C., and Conrath, U. (2018). Sulforaphane modifies histone H3, unpacks chromatin, and primes defense. Plant Physiol. **176:** 2395–2405.

Schölkopf, B.S., Alexander, J. (2022). *Learning with Kernels: Support Vector Machines, Regularization, Optimization, and Beyond*. MIT Press, Cambridge.

Schouveiler, P., Liew, L.C., Corso, M., Rajjou, L., Zinsmeister, J., and Lewsey, M.G. (2025). Deciphering seed development and germination in the single-cell era. Seed Sci. Res. **35:** 9–18.

Schumann, U., Lee, J.M., Smith, N.A., Zhong, C., Zhu, J.K., Dennis, E.S., Millar, A.A., and Wang, M.B. (2019). DEMETER plays a role in DNA demethylation and disease response in somatic tissues of Arabidopsis. Epigenetics **14:** 1074–1087.

Schwachtje, J., Whitcomb, S.J., Firmino, A.A.P., Zuther, E., Hincha, D.K., and Kopka, J. (2019). Induced, imprinted, and primed responses to changing environments: Does metabolism store and process information? Front. Plant Sci. **10:** 106.

Shaik, R., and Ramakrishna, W. (2012). Bioinformatic analysis of epigenetic and microRNA mediated regulation of drought responsive genes in rice. PLoS ONE **7:** e49331.

Sharma, G., Aminedi, R., Saxena, D., Gupta, A., Banerjee, P., Jain, D., and Chandran, D. (2019). Effector mining from the *Erysiphe pisi* haustorial transcriptome identifies novel candidates involved in pea powdery mildew pathogenesis. Mol. Plant Pathol. **20:** 1506–1522.

Sharma, M., Kumar, P., Verma, V., Sharma, R., Bhargava, B., and Irfan, M. (2022). Understanding plant stress memory response for abiotic stress resilience: Molecular insights and prospects. Plant Physiol. Biochem. **179:** 10–24.

Sheikh, A.H., Nawaz, K., Tabassum, N., Almeida-Trapp, M., Mariappan, K.G., Alhoraibi, H., Rayapuram, N., Aranda, M., Groth, M., and Hirt, H. (2023). Linker histone H1 modulates defense priming and immunity in plants. Nucl. Acids Res. **51:** 4252–4265.

Sheikh, M., Iqra, F., Ambreen, H., Pravin, K.A., Ikra, M., and Chung, Y.S. (2024). Integrating artificial intelligence and high-throughput phenotyping for crop improvement. J. Int. Agric. **23:** 1787–1802.

Shen, L., Ma, J., Li, P., Wu, Y., and Yu, H. (2023). Recent advances in the plant epitranscriptome. Genome Biol. **24:** 43.

Shibu, S.K., and Salim, A. (2023). Prediction of RNA binding proteins from amino acid sequences using machine learning techniques. In *2023 International Conference on Power, Instrumentation, Control and Computing (PICC)*. (Thrissur: IEEE) pp. 1–8.

Shoaib, Y., Usman, B., Kang, H., and Jung, K.H. (2022). Epitranscriptomics: An additional regulatory layer in plants' development and stress response. Plants **11:** 1033.

Singh, A., Jones, S., Ganapathysubramanian, B., Sarkar, S., Mueller, D., Sandhu, K., and Nagasubramanian, K. (2021). Challenges and opportunities in machine-augmented plant stress phenotyping. Trends Plant Sci. **26:** 53–69.

Singh, P., Yekondi, S., Chen, P.W., Tsai, C.H., Yu, C.W., Wu, K., and Zimmerli, L. (2014). Environmental history modulates Arabidopsis pattern-triggered immunity in a HISTONE ACETYLTRANSFERASE1–dependent manner. Plant Cell **26:** 2676–2688.

Smet, D., Opdebeeck, H., and Vandepoele, K. (2023). Predicting transcriptional responses to heat and drought stress from genomic features using a machine learning approach in rice. Front. Plant Sci. **14:** 1212073.

Sokolova, M., and Lapalme, G. (2009). A systematic analysis of performance measures for classification tasks. Inform. Process. Manag. **45:** 427–437.

Song, J., Angel, A., Howard, M., and Dean, C. (2012). Vernalization—A cold-induced epigenetic switch. J. Cell Sci. **125:** 3723–3731.

Song, T., Markham, K.K., Li, Z., Muller, K.E., Greenham, K., and Kuang, R. (2022). Detecting spatially co-expressed gene clusters with functional coherence by graph-regularized convolutional neural network. Bioinformatics **38:** 1344–1352.

Statello, L., Guo, C.J., Chen, L.L., and Huarte, M. (2021). Gene regulation by long non-coding RNAs and its biological functions. Nat. Rev. Mol. Cell Biol. **22:** 96–118.

Sun, L., Xu, K., Huang, W., Yang, Y.T., Li, P., Tang, L., Xiong, T., and Zhang, Q.C. (2021). Predicting dynamic cellular protein–RNA interactions by deep learning using in vivo RNA structures. Cell Res. **31:** 495–516.

Sun, S., Ye, X., and Zou, Q. (2023). Editorial: Machine learning on understanding the epigenetic mechanisms underlying plant adaptation and domestication. Front. Plant Sci. **14:** 1236787.

Tabe-Bordbar, S., and Sinha, S. (2023). Integrative modeling of lncRNA-chromatin interaction maps reveals diverse mechanisms of nuclear retention. BMC Genomics **24:** 395.

Taguchi, Y.-H. (2023). Bioinformatic tools for epitranscriptomics. Am. J. Physiol.: Cell Physiol. **324:** 447–457.

Tahir, M., Norouzi, M., Khan, S.S., Davie, J.R., Yamanaka, S., and Ashraf, A. (2024). Artificial intelligence and deep learning algorithms for epigenetic sequence analysis: A review for epigeneticists and AI experts. Comput. Biol. Med. **183:** 109302.

The Business Research Company. (2025). Artificial Intelligence (AI) in omics studies market analysis: Key insights on growth rates, trends, and major opportunities. *Latest Global Market Insight*. Company TBR. https://blog.tbrc.info/ (accessed on 26 April 2025).

Tian, X.C., Chen, Z.Y., Nie, S., Shi, T.L., Yan, X.M., Bao, Y.T., Li, Z.C., Ma, H.Y., Jia, K.H., Zhao, W., et al. (2024). Plant-LncPipe: A computational pipeline providing significant improvement in plant lncRNA identification. Hortic. Res. **11:** uhae041.

Townshend, R.J., Eismann, S., Watkins, A.M., Rangan, R., Karelina, M., Das, R., and Dror, R.O. (2021). Geometric deep learning of RNA structure. Science **373:** 1047–1051.

Tripathi, A., Tiwari, R.K., and Tiwari, S.P. (2022). A deep learning multi-layer perceptron and remote sensing approach for soil health-based crop yield estimation. Int. J. Appl. Earth Obs. Geoinf. **113:** 102959.

Turgut-Kara, N., Arikan, B., and Celik, H. (2020). Epigenetic memory and priming in plants. Genetica **148:** 47–54.

Ueda, M., and Seki, M. (2020). Histone modifications form epigenetic regulatory networks to regulate abiotic stress response. Plant Physiol. **182:** 15–26.

Vakilian, K.A. (2020). Machine learning improves our knowledge about miRNA functions towards plant abiotic stresses. Sci. Rep. **10:** 3041.

Vakulenko, S., and Grigoriev, D. (2021). Deep gene networks and response to stress. Mathematics **9:** 3028.

Van Dooren, T.J.M., Silveira, A.B., Gilbault, E., Jiménez-Gómez, J.M., Martin, A., Bach, L., Tisné, S., Quadrana, L., Loudet, O., and Colot, V. (2020). Mild drought in the vegetative stage induces phenotypic, gene expression, and DNA methylation plasticity in Arabidopsis but no transgenerational effects. J. Exp. Bot. **71:** 3588–3602.

van Loon, L.C. (2016). The intelligent behavior of plants. Trends Plant Sci. **21:** 286–294.

Vanden Broeck, A., Cox, K., Brys, R., Castiglione, S., Cicatelli, A., Guarino, F., Heinze, B., Steenackers, M., and Vander Mijnsbrugge, K. (2018). Variability in DNA methylation and generational plasticity in the Lombardy poplar, a single genotype worldwide distributed since the eighteenth century. Front. Plant Sci. **9:** 1635.

Varotto, S., Tani, E., Abraham, E., Krugman, T., Kapazoglou, A., Melzer, R., Radanović, A., and Miladinović, D. (2020). Epigenetics: Possible applications in climate-smart crop breeding. J. Exp. Bot. **71:** 5223–5236.

Veley, K.M., Elliott, K., Jensen, G., Zhong, Z., Feng, S., Yoder, M., Gilbert, K.B., Berry, J.C., Ghoshal, B., Bartolomé, J.G., et al. (2023). Improving cassava bacterial blight resistance by editing the epigenome. Nat. Commun. **14:** 85.

Voinnet, O. (2005). Non-cell autonomous RNA silencing. FEBS Lett. **579:** 5858–5871.

Waheed, S., Anwar, M., Saleem, M.A., Wu, J., Tayyab, M., and Hu, Z. (2021). The critical role of small RNAs in regulating plant innate immunity. Biomolecules **11:** 184.

Wang, D., Wang, Z., Chen, L., Xiao, H., and Yang, B. (2023b). Cross-parallel transformer: Parallel ViT for medical image segmentation. Sensors **23:** 9488.

Wang, G., Li, H., Ye, C., He, K., Liu, S., Jiang, B., Ge, R., Gao, B., Wei, J., Zhao, Y., et al. (2024). Quantitative profiling of 6mA at single base resolution across the life cycle of rice and Arabidopsis. Nat. Commun. **15:** 4881.

Wang, L., and Han, H. (2024). Strategies for improving the genome-editing efficiency of class 2 CRISPR/Cas system. Heliyon **10:** e38588.

Wang, R., Bashyam, V., Yang, Z., Yu, F., Tassopoulou, V., Chintapalli, S.S., Skampardoni, I., Sreepada, L.P., Sahoo, D., Nikita, K., et al. (2023a). Applications of generative adversarial networks in neuroimaging and clinical neuroscience. NeuroImage **269:** 119898.

Wang, Y., Deng, Y., Zheng, Y., Chattopadhyay, P., and Wang, L. (2025). Vision transformers for image classification: A comparative survey. Technologies **13:** ew 32.

Wang, Y., Hu, Q., Wu, Z., Wang, H., Han, S., Jin, Y., Zhou, J., Zhang, Z., Jiang, J., Shen, Y., et al. (2017). HISTONE DEACETYLASE 6 represses pathogen defence responses in *Arabidopsis thaliana*. Plant Cell Environ. **40:** 2972–2986.

Wang, Y., Zhang, P., Guo, W., Liu, H., Li, X., Zhang, Q., Du, Z., Hu, G., Han, X., Pu, L., et al. (2021a). A deep learning approach to automate whole-genome prediction of diverse epigenomic modifications in plants. New Phytol. **232:** 880–897.

Wang, Y., Zhang, P., Guo, W., Liu, H., Li, X., Zhang, Q., Du, Z., Hu, G., Han, X., Pu, L., et al. (2021b). A deep learning approach to automate whole-genome prediction of diverse epigenomic modifications in plants. New Phytol. **232:** 880–897.

Waryah, C.B., Moses, C., Arooj, M., and Blancafort, P. (2018). Zinc fingers, TALEs, and CRISPR systems: A comparison of tools for epigenome editing. Met. Mol. Biol. **1767:** 19–63.

Wei, J., Chen, S., Zong, L., Gao, X., and Li, Y. (2022). Protein–RNA interaction prediction with deep learning: Structure matters. Brief. Bioinform. **23:** bbab540.

Wei, L., Zhang, D., Xiang, F., and Zhang, Z. (2009). Differentially expressed miRNAs potentially involved in the regulation of defense mechanism to drought stress in maize seedlings. Int. J. Plant Sci. **170:** 979–989.

Weiberg, A., Wang, M., Lin, F.-M., Zhao, H., Zhang, Z., Kaloshian, I., Huang, H.-D., and Jin, H. (2013). Fungal small RNAs suppress plant immunity by hijacking host RNA interference pathways. Science **342:** 118–123.

Wibowo, A., Becker, C., Marconi, G., Durr, J., Price, J., Hagmann, J., Papareddy, R., Putra, H., Kageyama, J., Becker, J., et al. (2016). Hyperosmotic stress memory in Arabidopsis is mediated by distinct epigenetically labile sites in the genome and is restricted in the male germline by DNA glycosylase activity. eLife **5:** e13546.

Wilkinson, S.W., Hannan Parker, A., Muench, A., Wilson, R.S., Hooshmand, K., Henderson, M.A., Moffat, E.K., Rocha, P.S.C.F., Hipperson, H., Stassen, J.H.M., et al. (2023). Long-lasting memory of jasmonic acid-dependent immunity requires DNA demethylation and ARGONAUTE1. Nat. Plants. **9:** 81–95.

Wong, T.-T. (2015). Performance evaluation of classification algorithms by *k*-fold and leave-one-out cross validation. Pattern. Recognit. **48:** 2839–2846.

Wu, Z., Tang, J., Zhuo, J., Tian, Y., Zhao, F., Li, Z., Yan, Y., and Yang, R. (2019). Chromatin signature and transcription factor binding provide a predictive basis for understanding plant gene expression. Plant Cell Phys. **60:** 1471–1486.

Xie, Y., Chen, H., Tian, M., Wang, Z., Wang, L., Zhang, J., Wang, X., and Lian, C. (2024). Integrating multi-omics and machine learning survival frameworks to build a prognostic model based on immune function and cell death patterns in a lung adenocarcinoma cohort. Front. Immun. **15:** 1460547.

Xiong, L.Z., Xu, C.G., Saghai, Maroof, M.A., and Zhang, Q. (1999). Patterns of cytosine methylation in an elite rice hybrid and its parental lines, detected by a methylation-sensitive amplification polymorphism technique. Mol. Gen. Genet. **261:** 439–446.

Yadav, A., Mathan, J., Dubey, A.K., and Singh, A. (2024). The emerging role of non-coding RNAs (ncRNAs) in plant growth, development, and stress response signaling. Non-coding. RNA **10:** 13.

Yadav, N.S., Titov, V., Ayemere, I., Byeon, B., Ilnytskyy, Y., and Kovalchuk, I. (2022). Multigenerational exposure to heat stress induces phenotypic resilience, and genetic and epigenetic variations in *Arabidopsis thaliana* offspring. Front. Plant Sci. **13:** 728167.

Yamaguchi, N., Matsubara, S., Yoshimizu, K., Seki, M., Hamada, K., Kamitani, M., Kurita, Y., Nomura, Y., Nagashima, K., Inagaki, S., et al. (2021). H3K27me3 demethylases alter *HSP22* and *HSP17. 6C* expression in response to recurring heat in Arabidopsis. Nat. Commun. **12:** 1–16.

Yamashita, R., Nishio, M., Do, R.K.G., and Togashi, K. (2018). Convolutional neural networks: An overview and application in radiology. Insights Imaging **9:** 611–629.

Yan, Q., Wu, F., Yan, Z., Li, J., Ma, T., Zhang, Y., Zhao, Y., Wang, Y., and Zhang, J. (2019). Differential co-expression networks of long non-coding RNAs and mRNAs in *Cleistogenes songorica* under water stress and during recovery. BMC Plant Biol. **19:** 1–9.

Yang, H., Cui, Y., Feng, Y., Hu, Y., Liu, L., and Duan, L. (2023). Long non-coding RNAs of plants in response to abiotic stresses and their regulating roles in promoting environmental adaption. Cells **12:** 729.

Yang, P. (2025). Exploring Self-Organizing Maps: Applications in omics data analysis and integration with a generative model. Doctoral Dissertation, West Lafayette, Purdue University.

Yang, X., Sanchez, R., Kundariya, H., Maher, T., Dopp, I., Schwegel, R., Virdi, K., Axtell, M.J., and Mackenzie, S.A. (2020). Segregation of an MSH1 RNAi transgene produces heritable non-genetic memory in association with methylome reprogramming. Nat. Commun. **11:** 2214.

Yin, J., Ren, W., Fry, E.L., Sun, S., Han, H., and Guo, F. (2023). DNA methylation mediates overgrazing-induced clonal transgenerational plasticity. Sci. Total Environ. **897:** 165338.

Yin, M., Wang, S., Wang, Y., Wei, R., Liang, Y., Zuo, L., Huo, M., Huang, Z., Lang, J., Zhao, X., et al. (2024). Impact of abiotic stress on rice and the role of DNA methylation in stress response mechanisms. Plants **13:** 2700.

Yu, H., Qi, Y., and Ding, Y. (2022). Deep Learning in RNA structure studies. Front. Mol. Biosci. **9:** 869601.

Yu, X., Jiang, L., Jin, S., Zeng, X., and Liu, X. (2021). preMLI: A pre-trained method to uncover microRNA–lncRNA potential interactions. Brief. Bioinform. **23:** bbab470.

Yung, W.S., Li, M.W., Sze, C.C., Wang, Q., and Lam, H.M. (2021). Histone modifications and chromatin remodelling in plants in response to salt stress. Phys. Plant **173:** 1495–1513.

Zemlianskaia, N., Gauderman, W.J., and Lewinger, J.P. (2022). A scalable hierarchical lasso for gene-environment interactions. J. Comput. Graph. Stat. **31:** 1091–1103.

Zha, S., Yang, C., Zeng, X., Li, Z., Wang, Y., Yuan, H., Yu, M., and Xu, Q. (2021). Comparative analysis of H3K4 and H3K27 trimethylations in two contrasting *Tibetan hulless* barely varieties on powdery mildew infection. J. Plant Pathol. **103:** 117–126.

Zhai, J., Song, J., Cheng, Q., Tang, Y., and Ma, C. (2018). PEA: An integrated R toolkit for plant epitranscriptome analysis. Bioinformatics **34:** 3747–3749.

Zhan, J., and Meyers, B.C. (2023). Plant small RNAs: Their biogenesis, regulatory roles, and functions. Annu. Rev. Plant Biol. **74:** 21–51.

Zhang, H., and Shafiq, M.O. (2024). Survey of transformers and towards ensemble learning using transformers for natural language processing. J. Big Data **11:** 25.

Zhang, Q., Liang, Z., Cui, X., Ji, C., Li, Y., Zhang, P., Liu, J., Riaz, A., Yao, P., Liu, M., et al. (2018). N6-methyladenine DNA methylation in Japonica and Indica rice genomes and its association with gene expression, plant development, and stress responses. Mol. Plant **11:** 1492–1508.

Zhang, T., Zhao, Y.-L., Zhao, J.-H., Wang, S., Jin, Y., Chen, Z.-Q., Fang, Y.-Y., Hua, C.-L., Ding, S.-W., and Guo, H.-S. (2016). Cotton plants export microRNAs to inhibit virulence gene expression in a fungal pathogen. Nat. Plants **2:** 16153.

Zhang, X., Ibrahim, Z., Khaskheli, M.B., Raza, H., Zhou, F., and Shamsi, I.H. (2024). Integrative approaches to abiotic stress management in crops: Combining bioinformatics educational tools and artificial intelligence applications. Sustainability **16:** 7651.

Zhang, Y., Li, D., Zhang, H., Hong, Y., Huang, L., Liu, S., Li, X., Ouyang, Z., and Song, F. (2015). Tomato histone H2B monoubiquitination enzymes SlHUB1 and SlHUB2 contribute to disease resistance against *Botrytis cinerea* through modulating the balance between SA-and JA/ET-mediated signaling pathways. BMC Plant Biol. **15:** 1–20.

Zhang, Y., Si, F., Wang, Y., Liu, C., Zhang, T., Yuan, Y., and Gai, S. (2020). Application of 5-azacytidine induces DNA hypomethylation and accelerates dormancy release in buds of tree peony. Plant Physiol. Biochem. **147:** 91–100.

Zhao, D., Zhong, G., and Song, G. (2020a). Transfer of endogenous small RNAs between branches of scions and rootstocks in grafted sweet cherry trees. PLoS ONE **15:** e0236376.

Zhao, J., Sykacek, P., Bodner, G., and Rewald, B. (2018). Root traits of European *Vicia faba* cultivars—Using machine learning to explore adaptations to agroclimatic conditions. Plant Cell Environ. **41:** 1984–1996.

Zhao, T., Wu, H., Wang, X., Zhao, Y., Wang, L., Pan, J., Mei, H., Han, J., Wang, S., Lu, K., et al. (2023). Integration of eQTL and machine learning to dissect causal genes with pleiotropic effects in genetic regulation networks of seed cotton yield. Cell Rep. **42:** 113111.

Zhao, W., Lai, X., Liu, D., Zhang, Z., Ma, P., Wang, Q., Zhang, Z., and Pan, Y. (2020b). Applications of support vector machine in genomic prediction in pig and maize populations. Front. Genet. **11:** 598318.

Zheng, X., Chen, L., Li, M., Lou, Q., Xia, H., Wang, P., Li, T., Liu, H., and Luo, L. (2013). Transgenerational variations in DNA methylation induced by drought stress in two rice varieties with distinguished difference to drought resistance. PLoS ONE **8:** e80253.

Zhong, Z.D., Xie, Y.Y., Chen, H.X., Lan, Y.L., Liu, X.H., Ji, J.Y., Wu, F., Jin, L., Chen, J., Mak, D.W., et al. (2023). Systematic comparison of tools used for m6A mapping from nanopore direct RNA sequencing. Nat. Commun. **14:** 1906.

Zhou, H., Wang, F., and Tao, P. (2018). t-Distributed stochastic neighbor embedding method with the least information loss for macromolecular simulations. J. Chem. Theory Comput. **14:** 5499–5510.

Zi, N., Ren, W., Guo, H., Yuan, F., Liu, Y., and Fry, E. (2024). DNA methylation participates in drought stress memory and response to drought in *Medicago ruthenica*. Genes **15:** 1286.

Zou, B., Sun, Q., Zhang, W., Ding, Y., Yang, D.L., Shi, Z., and Hua, J. (2017). The Arabidopsis chromatin-remodeling factor CHR5 regulates plant immune responses and nucleosome occupancy. Plant, Cell Physiol. **58:** 2202–2216.

Zou, Y., Wang, Y., and Lu, X. (2023). Auto-encoding generative adversarial networks towards mode collapse reduction and feature representation enhancement. Entropy **25:** 1657.

SUPPORTING INFORMATION

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Table S1. Glossary of AI-based tools used or suggested for plant epigenetic analysis