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Review

Integrative Approaches to Abiotic Stress Management in Crops: Combining Bioinformatics Educational Tools and Artificial Intelligence Applications

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Abstract: Abiotic stresses, including drought, salinity, extreme temperatures and nutrient deficiencies, pose significant challenges to crop production and global food security. To combat these challenges, the integration of bioinformatics educational tools and AI applications provide a synergistic approach to identify and analyze stress-responsive genes, regulatory networks and molecular markers associated with stress tolerance. Bioinformatics educational tools offer a robust framework for data collection, storage and initial analysis, while AI applications enhance pattern recognition, predictive modeling and real-time data processing capabilities. This review uniquely integrates bioinformatics educational tools and AI applications, highlighting their combined role in managing abiotic stress in plants and crops. The novelty is demonstrated by the integration of multiomics data with AI algorithms, providing deeper insights into stress response pathways, biomarker discovery and pattern recognition. Key AI applications include predictive modeling of stress resistance genes, gene regulatory network inference, omics data integration and real-time plant monitoring through the fusion of remote sensing and AI-assisted phenomics. Challenges such as handling big omics data, model interpretability, overfitting and experimental validation remain there, but future prospects involve developing user-friendly bioinformatics educational platforms, establishing common data standards, interdisciplinary collaboration and harnessing AI for real-time stress mitigation strategies in plants and crops. Educational initiatives, interdisciplinary collaborations and trainings are essential to equip the next generation of researchers with the required skills to utilize these advanced tools effectively. The convergence of bioinformatics and AI holds vast prospects for accelerating the development of stress-resilient plants and crops, optimizing agricultural practices and ensuring global food security under increasing ‘environmental pressures. Moreover, this integrated approach is crucial for advancing sustainable agriculture and ensuring global food security amidst growing environmental challenges.

Keywords: abiotic stress; environment; bioinformatics educational tools; artificial intelligence; crop stress biology; crop improvement; sustainable agriculture

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1. Introduction

Global climate change (GCC) causes major environmental disturbances that could have harmful effects on the survival of all life forms across different biomes [1]. Experts predict that the global population will hit 9.1 billion by 2050, necessitating a 60–70% increase in crop production to satisfy the increasing food demand [2]. The natural growth and development mechanisms of sessile plants are inherently and evolutionarily aligned with circadian rhythms and changing environmental conditions [3,4]. Zhou et al. [5] explained that the emergence of the Internet of Things and the digital revolution has led to the rapid collection and transfer of huge amounts of data in real-time. This phenomenon, often referred to as "big data", can greatly impact various aspects of the food industry, which is directly and indirectly related to the plant industry; the integration of big data analytics with AI in the food industry and bioinformatics in agriculture enhances food safety, optimizes resource use, and improves crop resilience by enabling real-time monitoring, data-driven decision-making, and predictive analytics, thereby ensuring food security and sustainable agricultural practices. On the flip side, abiotic stresses present significant obstacles to sustainable agriculture, resulting in considerable reductions in crop yield and quality [6–8]. Educational initiatives and capacity-building programs are essential for equipping upcoming scientists and agricultural professionals with the skills and knowledge needed for bioinformatics and AI applications [9]. Interdisciplinary collaboration and knowledge transfer are critical for bridging the gap between biologists, computer scientists, and agricultural experts, facilitating the integration of bioinformatics and AI in managing abiotic stress [10]. Educational programs that develop a skilled workforce proficient in bioinformatics tools, databases, and AI applications are vital for driving innovation and addressing global food security challenges exacerbated by environmental pressures [11,12]. Significant expenses, laborious processes, and reductions in genetic diversity have hindered the development of resistant crops. Additionally, the control of multiple traits by a single gene and the unpredictable impact of environmental stimuli on signaling cascades have made success elusive. To ensure global food security, a comprehensive approach that includes omics techniques, speed breeding, and traditional crop development methods capable of thriving in any environment is necessary. This multi-pronged approach will pave the way for a future free from hunger [13–18].

To generate the literature for this review, a comprehensive search was conducted across multiple scientific databases/search engines, including Google Scholar, PubMed, Web of Science, and Scopus. The search strategy involved the use of specific keywords and phrases related to the focus of this review. Keywords included "abiotic stress", "crop improvement", "bioinformatics tools", "artificial intelligence in agriculture", "omics techniques", "transcriptomics", "genomics", "proteomics", "phenomics", "metabolomics", "machine learning", and "deep learning". Boolean operators such as AND, OR, and NOT were used to refine the search results and ensure the inclusion of pertinent studies. Additionally, reference lists of selected papers were reviewed to identify further pertinent studies. Producing plants and crops that can withstand stress conditions without significant yield penalties is essential. In this context, the combination of bioinformatics tools and artificial intelligence (AI) applications has emerged as a potent approach to addressing the complex problem of abiotic stress management in crops [15]. The novelty of this review lies in its unique integration of AI applications and bioinformatics tools, offering a holistic approach to enhancing the development of stress-resilient crops. This integration is crucial for advancing sustainable agriculture and ensuring global food security amidst the growing challenges posed by climate change. The search was limited to peer-reviewed English articles to ensure the reliability of the data and quality. In total, over 300 papers were studied for this review, carefully selected for their relevance and contribution to the understanding and advancement of stress-resilient crop development and sustainable agricultural practices. The objectives of this review are (i) to explore the synergistic integration of bioinformatics tools and AI applications for managing abiotic stress in plants and crops, (ii) to discuss the practical applications and benefits of this integration in enhancing crop resilience and productivity, and (iii) to address the challenges and outline future prospects for leveraging bioinformatics and AI in agricultural research. By focusing on these objectives, this review seeks to offer a thorough understanding of how the convergence of bioinformatics and AI can accelerate the development of stress-resilient crops, optimize agricultural practices, and ensure global food security under increasing environmental pressures.

2. Computational Biological Tools and Databases for Crop Improvement Research

Advances in molecular biology, genomics, and bioinformatics have generated massive biological datasets that require sophisticated computational analyses to derive meaningful insights [19–21]. Figure 1 illustrates the integration of various tools, techniques, and approaches in plant and crop improvement programs. This integration is essential for addressing complex biological questions related to abiotic stress, which often require multifaceted approaches for comprehensive understanding. Bioinformatics tools such as STRING and KEGG can be utilized to map and analyze oxidative stress-related pathways, including the accumulation of reactive oxygen species (ROS), which are crucial for understanding stress signaling and tolerance mechanisms. These tools enable the identification of genes and regulatory networks involved in ROS production and detoxification, highlighting their roles in stress responses. Tools such as BLAST and ClustalW are foundational for a detailed analysis of genome sequences through sequence alignment and comparison, which are crucial for understanding the genetic basis of stress responses in plants. These analyses help identify genes linked with stress tolerance and their regulatory mechanisms [22]. However, their effectiveness relies on the user’s familiarity with alignment algorithms and command-line operations, so new researchers may benefit from simpler, guided interfaces available in integrated platforms such as Ensembl Plants and PlantGDB, although they may have limitations in advanced customization and performance of large-scale data. Bioinformatics tools that integrate genetic and epigenetic data, such as EpiDiverse and MethGo [23], enable researchers to explore how epigenetic modifications such as DNA methylation and histone modifications interact with genetic variants. This combined approach helps in identifying key regulatory elements that influence gene expression and plant stress responses. Surrounding the central hub are components and methodologies, including genomic analysis (GWAS, population genetics, and molecular breeding), genotyping technologies (SNP genotyping and NGS analysis), breeding strategies (multi-parent advanced generation cross and genome selection), and statistical analyses. These elements form a comprehensive framework for leveraging cutting-edge technologies and data-driven approaches to develop stress-resistant and high-yielding crop varieties [24].

Bioinformatics is an interdisciplinary field that merges the elements of mathematics, computer science, statistics, and life sciences, playing a vital role in managing, analyzing, and interpreting large volumes of biological data. This field systematically develops and applies computational tools for the purposes of data collection, mining, storage, database searches, analyses, interpretation, modeling, and product design [25–27]. Its applications in plant improvement are extensive, providing tools and technologies to support and assess research, enabling complementary computational tools and database development, and interpreting biological information to enhance the understanding of biological systems [28]. Powerful bioinformatics tools are available for structural, functional, and sequence analyses and database construction [29], as well as facilitating genomic information-assisted crop breeding and improvement programs, enabling the exploitation of vast genetic information from sequencing projects to improve crop traits [30,31]. However, some researchers remain unfamiliar with these tools, leading to potential misinterpretation and underutilization of available data resources. Next-generation sequencing (NGS) tools enable swift sequencing but introduce challenges in analyzing millions or billions of short DNA reads [32], necessitating computational algorithms and software development for processing genotypes, genetic maps, and gene expression data to extract biological insights [33]. User-friendly interfaces provide access to outcomes generated by these algorithms through websites, databases, and software tools (Table 1). The Omics era has advanced plant system understanding through tools such as genomics, proteomics, transcriptomics, and metabolomics, with data integration across these levels offering a holistic view of molecular interactions leading plant responses to abiotic stress [34].

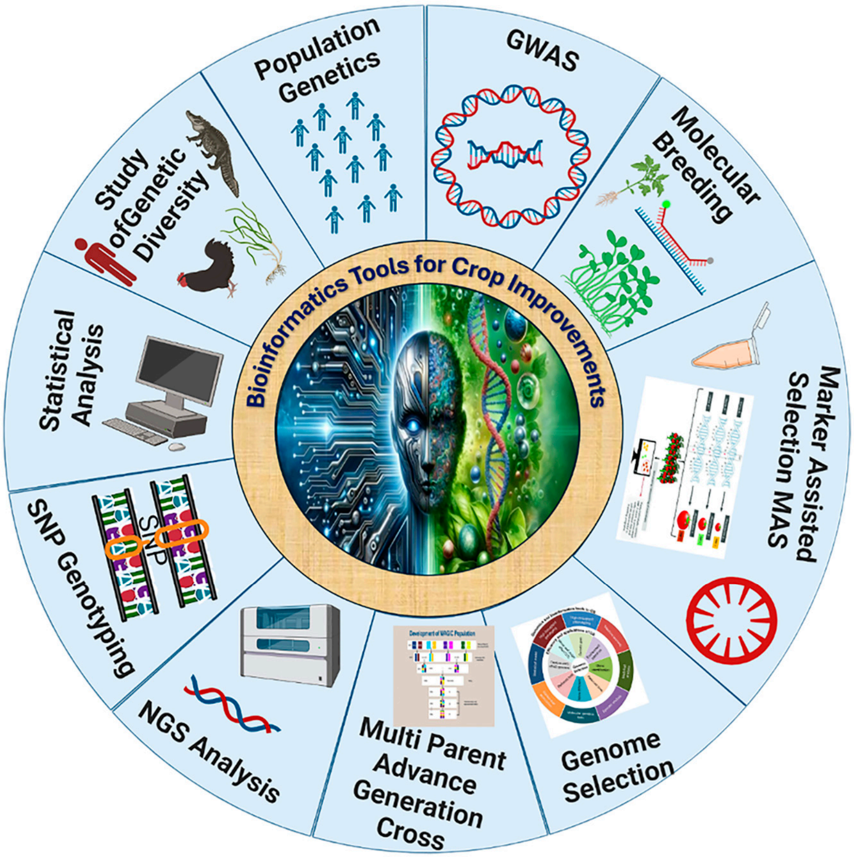


Figure 1. Integrated bioinformatics educational tools and approaches for crop improvement.

Table 1. Bioinformatics databases for plant stress and crop improvement. Modified from [12,20,35–43].

Databases	Features/Description/Function	Website Links
AtMAD	Provides omics data of *Arabidopsis thaliana*	http://www.megabionet.org/atmad (accessed on 28 Feburary 2024)
GoMapMan	Functional annotation of plant-related genes	http://www.gomapman.org/ (accessed on 4 March 2024)
PGDBj	Database for DNA markers and their linkage	http://pgdbj.jp/en/index (accessed on 1 March 2024)
Phytozome	A comparative genomics database for plants	https://phytozome-next.jgi.doe.gov/ (accessed on 3 March 2024)
PlantGDB	A genomics database that provides annotated transcript assemblies for >100 plant (Viridiplantae) species	http://www.plantgdb.org/ (accessed on 22 Feburary 2024)
PMRD	Plant miRNA database	http://bioinformatics.cau.edu.cn/PMRD/ (accessed on 5 March 2024)
SALAD	Compares proteomic data across different species	https://salad.dna.affrc.go.jp/salad/en/ (accessed on 8 March 2024)
FastQC	Quality checks on raw sequence data coming from high-throughput sequencing pipelines	https://www.bioinformatics.babraham.ac.uk/projects/fastqc/ (accessed on 28 Feburary 2024)
Bowtie2	Aligns sequencing reads in an ultrafast and memory-efficient manner	http://bowtie-bio.sourceforge.net/bowtie2/index.shtml (accessed on 28 Feburary 2024)
kngMap	Aligns long reads to a reference sequence	https://github.com/zhang134/kngMap (accessed on 2 March 2024)
MOSAIK	Maps 2nd- and 3rd-generation sequencing reads	https://github.com/wanpinglee/MOSAIK (accessed on 1 March 2024)
Novoalign	Maps short reads onto a reference genome from different NGS platforms	http://www.novocraft.com/products/novoalign/ (accessed on 29 Feburary 2024)

Table 1. *Cont.*

Databases	Features/Description/Function	Website Links
SOAP3-dp	First short-read alignment tool that leverages the multiprocessors in a graphic processing unit (GPU) to achieve a drastic improvement in speed.	http://soap.genomics.org.cn/ (accessed on 3 March 2024)
Minimap2	Accurate and efficient for long, noisy RNA and genomic sequences	https://github.com/lh3/minimap2 (accessed on 26 March 2024)
GATK	Bioinformatics tool set for analyzing high-throughput sequencing and variant call format data	https://software.broadinstitute.org/gatk/ (accessed on 26 Feburary 2024)
Freebayes	Excels at calling haplotype-based variants from a population	https://github.com/ekg/freebayes (accessed on 2 March 2024)
Platypus	A haplotype-based variant caller	https://www.rdm.ox.ac.uk/research/lunter-group/lunter-group/platypus-a-haplotype-based-variant-caller-for-next-generation-sequence-data (accessed on 6 March 2024)
IGV	A tool for high-performance interactive exploration of large, integrated genomic datasets	https://igv.org/ (accessed on 26 Feburary 2024)
VISTA	Utilizes global alignment strategies and a curve-based visualization technique and is also used for comparative analysis	https://genome.lbl.gov/vista/index.shtml (accessed on 2 March 2024)
R software	Gosling: A grammar for scalable and interactive visualization of genomic data	http://gosling-lang.org/ (accessed on 4 March 2024)
GET_HOMOLOGUES-EST	A highly customized and automated pipeline specifically designed for individuals with a non-bioinformatics background	https://github.com/eead-csic-compbio/get_homologues/releases (accessed on 4 March 2024)
PAN2HGENE	Computational tool that allows identification of gene products missing from the original genome sequence	https://sourceforge.net/projects/pan2hgene-software/ (accessed on 28 Feburary 2024)
Pantools	A versatile tool for mapping metagenomic and genomic reads in both prokaryotes and eukaryotes	https://git.wur.nl/bioinformatics/pantools (accessed on 2 March 2024)
PanViz	An interactive visualization tool for comparing individual genomes to the pangenome	https://github.com/thomasp85/PanViz/blob/master/package.json (accessed on 26 Feburary 2024)
ppsPCP	Detects presence-absence variations and assembles a comprehensive pangenome	http://cbi.hzau.edu.cn/ppsPCP/ (accessed on 1 March 2024)
RPAN	A rich source for rice genomic research and breeding	https://cgm.sjtu.edu.cn/3kricedb/ (accessed on 1 March 2024)
Hap10	A novel algorithm for haplotype assembly of polyploid genomes using linked reads	https://sourceforge.net/projects/sdhap/ (accessed on 8 March 2024)
HapCut2	Provides robust and accurate haplotype assembly for various sequencing technologies	https://github.com/vibansal/HapCUT2 (accessed on 23 Feburary 2024)
HaploConduct	A package designed for the reconstruction of individual haplotypes	https://github.com/HaploConduct/HaploConduct (accessed on 8 March 2024)
HAPLOVIEW	Analysis and visualization of linkage disequilibrium (LD) and haplotype maps	https://www.broadinstitute.org/haploview/haploview (accessed on 6 March 2024)
HapTree	Provides a polyploid haplotype assembly tool based on a statistical framework	http://cb.csail.mit.edu/cb/haptree/ (accessed on 27 Feburary 2024)
BFCounter	A program for counting k-mers in DNA sequence data	http://pritch.bsd.uchicago.edu/bfcounter.html (accessed on 2 March 2024)
iMOKA	Utilizes a fast and accurate feature reduction step	https://github.com/RitchieLabIGH/iMOKA (accessed on 3 March 2024)
KAT	A multi-purpose software toolkit for reference-free quality control (QC) of whole-genome sequencing (WGS) reads and de novo genome assemblies	https://github.com/TGAC/KAT (accessed on 28 Feburary 2024)
KITSUNE	Identifies the optimal k-mer length for alignment-free phylogenomic analysis	https://github.com/natapol/kitsune (accessed on 5 March 2024)
KmerGO	Identifies group-specific sequences using k-mers	https://github.com/ChnMasterOG/KmerGO (accessed on 3 March 2024)

Table 1. *Cont.*

Databases	Features/Description/Function	Website Links
CHOPCHOP	A web-based tool for selecting target sites for CRISPR/Cas9- or TALEN-directed mutagenesis (generating primers and displaying the chromosomal site)	https://chopchop.cbu.uib.no/ (accessed on 26 Feburary 2024)
CLD	Suitable for designing libraries using modified CRISPR enzymes and targeting non-coding regions	https://github.com/boutroslab/cld (accessed on 3 March 2024)
CRISPETa	Designs optimal pairs of sgRNAs for the deletion of desired genomic regions	http://crispeta.crg.eu/ (accessed on 3 March 2024)
CROPSR	Highly effective and efficient for designing gRNA in crops	https://github.com/H2muller/CROPSR (accessed on 2 March 2024)
BioNIX	Integrates the output of several programs, including BLAST, FEX, FGENE, GRAIL, GENEFINDER, HEXON, MZEF, POLYAH, REPEATMASKER, and TRNASCAN	https://en.wikipedia.org/wiki/List_of_gene_prediction_software#cite_note-37 (accessed on 27 Feburary 2024)
IntFOLD	A unified interface used for tertiary structure prediction/3D modeling, 3D model quality assessment, intrinsic disorder prediction, domain prediction, and prediction of protein–ligand binding residues	http://www.reading.ac.uk/bioinf/IntFOLD/ (accessed on 9 March 2024)
RaptorX	Performs protein 3D modeling, distant homology discovery, and binding site prediction	http://raptorx.uchicago.edu/ (accessed on 24 Feburary 2024)
ESyPred3D	Recognizes templates, aligns sequences, and performs 3D modeling	http://www.fundp.ac.be/urbm/bioin (accessed on 4 March 2024)
FoldX	Designs protein and performs energy calculations	http://foldx.crg.es/ (accessed on 4 March 2024)
Phyre and Phyre2	Used for remote template identification, alignment, 3D modeling, multi-template modeling, and ab initio studies	http://www.sbg.bio.ic.ac.uk/~phyre/ (accessed on 3 March 2024)
HHpred	Assists in template recognition, alignment, and 3D modeling	http://arquivo.pt/wayback/20160514083149/http://toolkit.tuebingen.mpg.de/hhpred (accessed on 3 March 2024)
MODELLER	Satisfies spatial restraints for protein structure modeling	https://salilab.org/modeller/ (accessed on 7 March 2024)
CAN FOLD	Satisfies contact and distance constraints for protein folding	https://github.com/multicom-toolbox/CONFOLD (accessed on 28 Feburary 2024)
MOE (Molecular Operating Environment)	Performs loop modeling, utilizes rotamer libraries for sidechain conformations and MM forcefields, identifies templates, uses multiple templates, and accounts for additional environments (e.g., excluded ligand volumes)	http://www.chemcomp.com/ (accessed on 2 March 2024)
ROBETTA	Uses Rosetta homology modeling and fragment assembly for Ginzu domain prediction	http://robetta.bakerlab.org/ (accessed on 1 March 2024)
BHAGEERATH-H	Predicts protein tertiary structure by combining methods of ab initio folding and homology modeling	http://www.scfbio-iitd.res.in/bhageerath/bhageerath_h.jsp (accessed on 4 March 2024)
SWISS-MODEL	Performs local similarity/fragment assembly for protein structure prediction	http://swissmodel.expasy.org/ (accessed on 29 Feburary 2024)
Yasara	Performs ligand and oligomer modeling, template detection, alignment, and model fragment hybridization, and can be used in text mode (clusters) or with a graphical user interface	http://www.yasara.org/ (accessed on 2 March 2024) http://www.yasara.org/casp8.htm (accessed on 1 March 2024)
AWSEM-Suite	Uses molecular dynamics simulation to understand co-evolutionarily history, template-guided, and optimized folding landscapes	http://awsem.rice.edu/ (accessed on 28 Feburary 2024)
Gramene	With a user-friendly interface, allows users to filter and export attributes related to species, germplasm, name/synonym, library/source and more.	http://www.gramene.org/ (accessed on 5 March 2024)

Table 1. *Cont.*

Databases	**Features/Description/Function**	**Website Links**
EnsemblPlants	Provides annotation, alignment, and visualization of plant genomes from biodiversity initiatives and collaborations	http://plants.ensembl.org/ (accessed on 1 March 2024)
MapGene2Chromosome	Analyzes the heredity of gene families and performs map-based gene cloning	http://mg2c.iask.in/mg2c_v2.0/ (accessed on 26 Feburary 2024)
MapChart	Produces charts of genetic linkage maps and QTL data	https://www.mapchart.net/ (accessed on 1 March 2024)
GSDS 2.0	Assists in visualizing annotated gene features and generating high-quality figures for publication	https://gsds.gao-lab.org/Gsds_help.php (accessed on 3 March 2024)
IUPred	Provides a combined web interface that identifies disordered protein regions using IUPred2 and disordered binding regions using ANCHOR2	https://iupred2a.elte.hu/ (accessed on 4 March 2024)
DESeq2	A fundamental task in RNA-seq count data analysis is detecting differentially expressed genes	https://bioconductor.org/packages/release/bioc/html/ (accessed on 26 Feburary 2024)
StringTie	Employs efficient algorithms to reconstruct transcript structures and estimate expression levels from bulk RNA-Seq reads aligned to a reference genome	https://ccb.jhu.edu/software/stringtie/ (accessed on 3 March 2024)
PLEXdb	A unified plant and associated pathogens gene expression resource that serves as a genotype-to-phenotype, hypothesis-building information warehouse. It leverages highly parallel expression data and provides access to pertinent genetic, physical, and pathway data	https://www.plexdb.org/ (accessed on 28 Feburary 2024)
PlantGenIE	A comprehensive web resource designed for searching, visualizing, and analyzing genomics as well as transcriptomics data across multiple plant species	http://www.plantgenie.org/ (accessed on 7 March 2024)
TAIR	A genetic and molecular biology database dedicated to *A. thaliana*	https://www.arabidopsis.org/ (accessed on 23 Feburary 2024)
MaizeGDB	Functions as a community-focused, long-term informatics resource tailored for researchers studying *Zea mays*	https://www.maizegdb.org/ (accessed on 2 March 2024)
Genevestigator	A tool for exploring public and private gene expression data from bulk tissue to single cells	https://genevestigator.com/ (accessed on 28 Feburary 2024)
MetaboAnalyst	Offers various modules for statistical, biomarker, pathway, network, and functional analysis of metabolomics data	https://www.metaboanalyst.ca/ (accessed on 4 March 2024)
XCMS	A framework designed for the processing and visualization of chromatographically separated and single-spectra mass spectral data	https://xcmsonline.scripps.edu/landing_page.php?pgcontent=mainPage (accessed on 4 March 2024)
MetaboLights	A cross-species, cross-technique database that encompasses metabolite structures, spectra, roles, locations, concentrations, and experimental data	https://www.ebi.ac.uk/metabolights/ (accessed on 3 March 2024)
PMN	Provides statistics on pathways, enzymes, reactions, and compounds, along with detailed descriptions	http://plantcyc.org/ (accessed on 27 Feburary 2024)
MassBank	A metadata-centric, auto-curating repository designed for efficient storage and querying of mass spectral data	https://massbank.eu/MassBank/ (accessed on 2 March 2024)
PlantCyc	Multi-species reference database of plant metabolic pathways in over 500 species	http://pmn.plantcyc.org/ (accessed on 27 Feburary 2024)
Golm Metabolome Database	Enables the search and distribution of mass spectra for biologically active metabolites quantified through Gas chromatography–mass spectrometry (GC–MS)	http://gmd.mpimp-golm.mpg.de/ (accessed on 3 March 2024)
COLOMBOS	Offers extensive organism-specific cross-platform gene expression datasets for various bacterial model organisms	http://colombos.net/ (accessed on 4 March 2024)

Table 1. *Cont.*

Databases	**Features/Description/Function**	**Website Links**
OmicsNet	Facilitates the interpretation of multi-omics signatures through biological networks	http://www.omicsnet.ca/ (accessed on 29 Feburary 2024)
OmicsDI	Open-source platform that integrates and disseminates omics datasets from various resources and studies	https://www.omicsdi.org/ (accessed on 5 March 2024)
OMICTools	Provides a comprehensive list of tools and databases for genomics applications	https://omictools.com/ (accessed on 5 March 2024)
Panorama	A server-based data repository application for targeted mass spectrometry assays that integrates with the Skyline mass spec workflow	https://panoramaweb.org/ (accessed on 28 Feburary 2024)
CRISPR RGEN Tools	Offers standalone, downloadable predictive models that efficiently forecast potential off-target numbers in CRISPR applications	https://www.rgenome.net/Cas-designer (accessed on 3 March 2024)
CRISPRscan	Generates tracks for genome browsers, designs sgRNAs for specific gene sites, and scans the entire genome for off-target effects	https://www.crisprscan.org/ (accessed on 27 Feburary 2024)
CCTop	Identifies mismatches, forecasts off-target effects, and predicts sgRNA efficiency	https://cctop.cos.uni-heidelberg.de:8043/ (accessed on 4 March 2024)
CRISTA	Provides a framework for ML, identifies off-targets, and evaluates targets	https://crista.tau.ac.il/ (accessed on 1 March 2024)
CRISPR-GE	Creates vectors and designs primers for on-target amplification	https://skl.scau.edu.cn/ (accessed on 1 March 2024)
CRISPR-P	Analyzes gRNA sequences and performs on-target and off-target screening	https://crispr.hzau.edu.cn/CRISPR2/ (accessed on 29 Feburary 2024)
CRSeek	Locates both on- and off-target websites	https://github.com/DamLabResources/crseek (accessed on 2 March 2024)
CRISPResso	Potential is found for both on- and off-targets	http://github.com/lucapinello/CRISPResso (accessed on 28 Feburary 2024)
Cas-OFFinder	Identifies potential off-target sites and provides detailed information about their locations, orientations, and the number of mismatches	http://www.rgenome.net/cas-offinder/ (accessed on 1 March 2024)
CasOT	Identifies potential off-target locations based on user-specified PAM types, mismatch rates, and genomes	http://eendb.zfgenetics.org/Casot/ (accessed on 28 Feburary 2024)
CRISPRitz	Enumerates, annotates, and assesses the potential implications of putative off-target sequences on the functioning genome	https://github.com/pinellolab/CRISPRitz (accessed on 1 March 2024)
CRISPRloci	Defines the CRISPR leaders for each locus, predicts the direction of each CRISPR array, and annotates Cas9 genes	https://rna.informatik.uni-freiburg.de (accessed on 28 Feburary 2024)
CRISPRdigger	Enhances the accuracy of a query genome by detecting CRISPRs with improved direct repeat annotations	http://www.healthinformaticslab.org/supp/ (accessed on 2 March 2024)
BATCH-GE	Identifies and documents precise genome editing events, such as indel mutations, and estimates the associated mutagenesis efficiencies	https://github.com/WouterSteyaert/BATCH-GE.git (accessed on 1 March 2024)
CRISPR Plant v2	For extremely specialized sgRNAs	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6330547/ (accessed on 1 March 2024)
CrisprGE	A central repository for CRISPR/Cas9-based genome editing data	http://crdd.osdd.net/servers/crisprge/ (accessed on 29 Feburary 2024)

2.1. Genomics

Plants' molecular response to stress encompasses complex interactions among genetic, transport, and metabolic processes [44–46]. High-throughput sequencing technologies revolutionized plant genomics, enabling budget-friendly and fast generation of extensive genetic data [47]. In managing abiotic stress, genomic approaches identified stress-responsive genes (SRGs), elucidated regulatory networks, and developed molecular markers for breeding programs [16]. At the genomic level, transcription factors, chromatin structure, and cis-regulatory DNA sequences primarily regulate plant stress [48]. Databases and computational tools play a crucial role in various aspects of sequence analysis, such as identifying orthologous genes, determining gene functions, phylogenetic analysis, mapping chromosomal location, studying introns, identifying cis-regulatory elements, and analyzing 5′ and 3′ untranslated regions [49]. Databases such as Gramene, Phytozome, Ensembl Plants, PlantGDB, and VISTA offer interfaces that are user-friendly and assist in retrieving plant genes/orthologous sequences, while databases such as riceDB, SoyBase, TAIR, and MaizeGDB provide valuable resources that are plant species-specific [49]. Tools such as MapGene2Chromosome v2, MapChart, GSDS 2.0, PIECE, IUPred, ProtParam, Tbtools, and PlantCARE aid in gene mapping, structure analysis, gene–gene interactions, and cis-regulatory element identification. Moreover, QTL genomics, pangenomics, structural genomics, comparative genomics, epigenomics, genome editing, synthetic genomics, phylogenomics, functional annotation, and genome-wide association studies (GWAS) contribute to a thorough understanding of genetic information and its applications [50,51]. GWAS has been crucial in identifying genetic variants associated with abiotic stress tolerance in crops [52]. Genomic tools not only identify genetic variations linked to stress tolerance but also, when combined with epigenomic data, provide insights into how epigenetic modifications regulate gene expression under stress conditions. For instance, the integration of GWAS data with DNA methylation patterns can reveal how epigenetic marks influence the expression of stress-responsive genes, thereby offering a more nuanced understanding of plant resilience [53,54]. These discoveries can create marker-assisted selection techniques for breeding stress-tolerant crop varieties. By exploring plant life's intricacies, these genomics branches provide valuable insights, driving progress in agriculture, ecology, and biotechnology [12].

2.2. Transcriptomics

Transcriptomics is the study of the entire set of RNA transcripts in specific cells or tissues under different conditions, providing insights into gene expression patterns, alternative splicing, and post-transcriptional modifications, which helps researchers understand the underlying molecular mechanisms, often revealing how plants regulate gene expression in response to oxidative stress, including genes involved in ROS production and scavenging [55]. For instance, Adil et al. [56] and Sehar et al. [57] conducted a transcriptomics study to investigate gene expression patterns in rice plants exposed to heavy metals (i.e., cadmium and arsenic), identifying key genes and regulatory pathways involved in stress responses. Commonly used tools and databases for plants include Cufflinks, which is used for transcript assembly, quantification, and differential expression analysis from RNA-Seq data, widely applied in crops such as *Arabidopsis* and rice [58]; DESeq2, commonly used in maize and wheat, aids in differential gene expression analysis (both DESeq2 and Cufflinks can help identify differentially expressed genes related to oxidative stress responses, providing insights into the plant's ability to manage ROS accumulation under various abiotic stresses) [59]; TopHat maps RNA-Seq reads to reference genomes and identifies splice junctions in soybean and barley [58]; StringTie facilitates transcript assembly and quantification in tomatoes. Plant Expression Database, PlantGenIE [60], *Arabidopsis* Information Resource [61], RiceXPro [62], MaizeGDB [63], and Genevestigator [64] are valuable resources for transcriptomics data and analysis across various plant species, including *Arabidopsis*, rice, maize, soybean, barley, tomato, and poplar. Transcriptomics tools such as DESeq2 and StringTie are powerful for differential expression analysis and transcript assembly but come with high computational requirements and steep learning curves. These challenges can be daunting for new researchers without extensive bioinformatics training. Conversely, platforms such as the *Arabidopsis* Information Resource (TAIR) and PlantGenIE provide more user-friendly interfaces, allowing beginners to explore transcriptomics data with less technical overhead, although they may not offer the same depth of analysis as command-line tools. Additionally, specialized omics disciplines such as epitranscriptomics in rice [65], non-coding RNA transcriptomics in *Arabidopsis* [66], single-cell transcriptomics in maize [67], and spatial transcriptomics in wheat [68] offer detailed insights into the dynamic nature of gene expression and RNA regulation. Combining genomic and transcriptomic data has significantly improved our knowledge of the intricate regulatory networks responsible for plant responses to abiotic stress. By merging information on genetic variation, gene expression, and regulatory elements, scientists can create more inclusive models of stress signaling and acclimation pathways, leading towards the development of stress-resistant crops through genetic engineering.

2.3. Proteomics

By studying alterations in gene expression and proteome profiles, the adaptive strategies employed by plants at both the cellular and metabolic levels can be determined [69,70]. For example, Wu et al. [71] utilized TMT-based quantitative proteomics to examine the alterations in water loss and cell wall metabolism during the postharvest withering of tobacco foliage, identifying key proteins involved in various metabolic pathways and underscoring the importance of cell wall metabolism and dehydration. Similarly, another study by Wu et al. [72] employed iTRAQ-based proteomics to investigate the molecular mechanisms behind pigment metabolism and tobacco leaf color changes during curing, identifying key proteins associated with carotenoid/chlorophyll metabolism. Feng et al. [73] utilized TMT-based proteomics to investigate proteome dynamics in plants under various abiotic stresses, identifying critical proteins and pathways that contribute to stress tolerance. Sagonda et al. [74] also employed iTRAQ-based proteomics to investigate protein expression profiles under abiotic stress, shedding light on the molecular mechanisms behind plant stress responses. In fact, to decode the complex proteomic details of plant stress responses, the scientific community has created specialized bioinformatics resources that aggregate data from various "-omics" studies, thus allowing efficient data mining and collaborative research [75,76]. Several valuable resources and databases (such as UniProtKB/Swiss-Prot, Plant Proteome Database, Araport, etc.) support plant proteomics research [77–79]. Moreover, PRIDE Database and Massive serve as repositories for mass spectrometry-oriented proteomics data, including plant-based experiments [80]. ProteomeXchange enables the distribution of proteomics data through multiple repositories [81]. Plant PTM Viewer aids in the exploration and visualization of post-translational protein modifications [82], while SUBA4 offers data on the subcellular localization of *Arabidopsis* proteins, aiding spatial proteomics investigations [83]. While there is a plethora of bioinformatics tools and databases available for plant research, their effective utilization often requires specialized training and knowledge. Proteomics databases such as UniProtKB/Swiss-Prot and the Plant Proteome Database offer comprehensive resources for protein data; however, they require users to navigate complex datasets and understand advanced proteomic concepts. User-friendly tools such as Plant PTM Viewer can help beginners visualize post-translational modifications without needing extensive background knowledge, although they might lack advanced data manipulation capabilities found in more specialized software. Therefore, user-friendly interfaces, online training resources, and educational platforms can facilitate the accessibility and understanding of these tools and databases for researchers, students, and professionals [35]. Interactive tutorials, video demonstrations, and step-by-step guides can aid in adopting and proficiently using bioinformatics resources, enabling seamless data analysis and interpretation [84]. Furthermore, the development of dedicated educational modules and workshops can provide hands-on training and foster a deeper understanding of the capabilities and applications of these tools in the context of abiotic stress management in plants and crops. Continuous progress has laid the groundwork for innovative techniques, which hold significant potential for tackling core biological inquiries [85]. One such example is spatial proteomics, which uses subcellular fractionation and purification methods. These techniques have significantly advanced our comprehension of specific proteomic activities within distinct plant organs and processes. This subdiscipline has been instrumental in uncovering the complex spatial patterns of proteins under abiotic stress conditions. Consequently, it has deepened our understanding of plant stress adaptation mechanisms [86].

2.4. Metabolomics

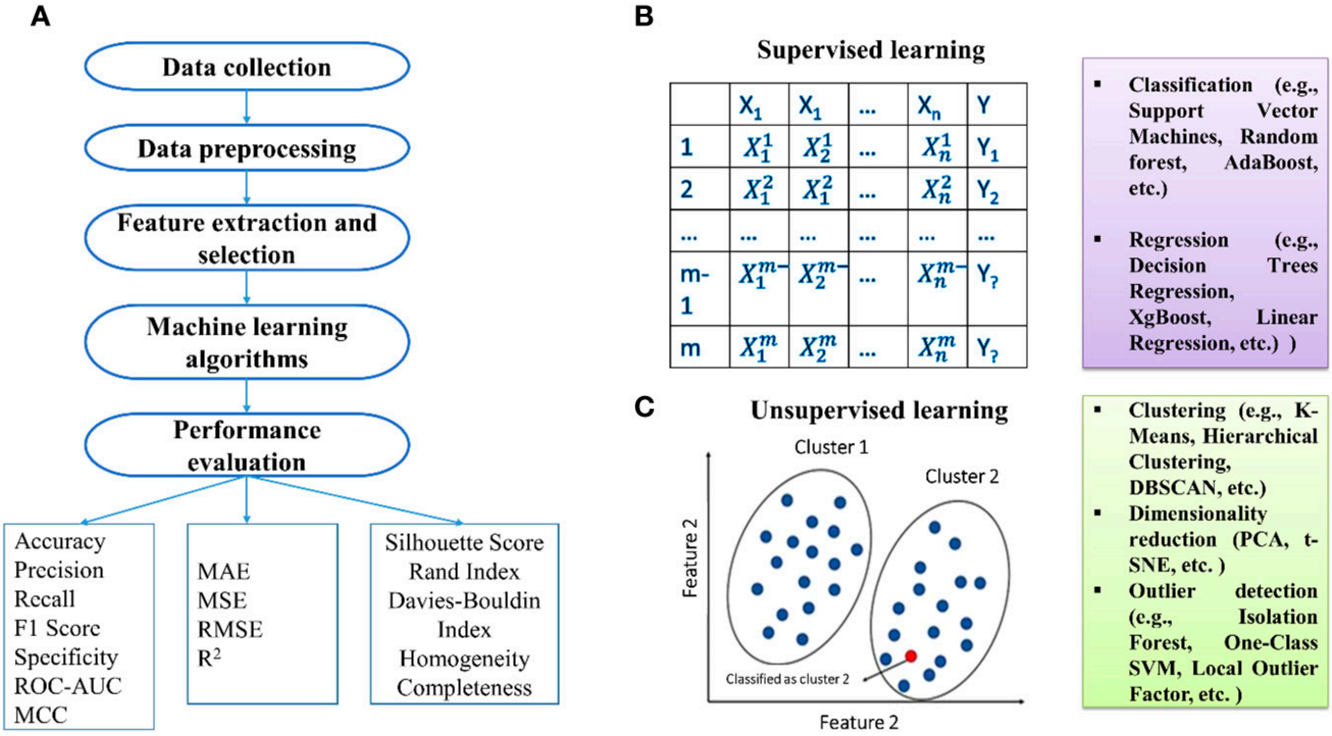
Metabolomics is a vital approach for studying complete metabolites/biochemical pathways in biological samples. For instance, Sehar et al. [87] conducted a metabolomics study to explore the metabolic changes in plants under heavy metal stress, providing detailed insights into the metabolic pathways and roles of specific metabolites in stress responses. Several tools and databases facilitate the analysis of such data, including MetaboAnalyst for data pre-processing, statistical analysis, pathway analysis, and visualization [88], XCMS for detecting, quantifying, and aligning metabolites [89], MetaboLights for sharing and integrating metabolomics data [90], Plant Metabolic Network for enzyme information, curated pathway databases, and metabolite annotations, Kyoto Encyclopedia of Genes and Genomes for integrating multi-omics data and providing metabolic pathway information [91], MassBank for plant metabolite data [92], PlantCyc for curated pathway information [93], Golm Metabolome Database for mass spectra, retention indices, and plant metabolite information [94], and McCloud for mass spectrometry data and spectral libraries [95]. Additionally, there are specialized omics disciplines such as lipidomics (lipid analysis) [96] and glycomics (carbohydrate analysis) [97]. High-throughput proteomic and metabolomic analyses involve the identification of stress-responsive proteins and metabolites, their post-translational modifications, and their interactions, which are essential for developing stress-tolerant crop varieties [98]. This multi-omics approach has enabled the identification of important regulatory centers, clarifying stress signaling pathways, and the discovery of novel stress-tolerance mechanisms. Ultimately, this contributes to developing better crop varieties [99]. Of note, tools such as MetaboAnalyst and XCMS provide detailed analysis capabilities for complex datasets but require a considerable level of expertise in data processing and interpretation. For novice users, starting with tools that offer guided workflows or simplified data inputs, such as KEGG for pathway analysis, can help bridge the gap, although these tools may not always provide the depth required for cutting-edge research.

3. Integrated Omics and Its Role in Addressing Crop Abiotic Stress

To comprehensively understand complex plant processes, integrating data from genomics, transcriptomics, proteomics, and metabolomics using bioinformatics and AI algorithms could prove to be useful [100,101]. A variety of tools and databases are available to aid in this regard; for example, COLOMBOS compares and visualizes multi-omics data from diverse plant experiments, facilitating cross-platform analysis and the exploration of co-regulated genes and functional modules [12,102]. Of note, OmicsDI integrates data from multiple omics studies, allowing researchers to explore and access publicly available datasets [103]. OMICTools offers a curated collection of databases and software tools designed for omics data analysis, supporting the integration of plant analysis and multi-omics data [104]. Plant Metabolomics provides resources for the analysis of plant metabolomics data, including databases, repositories, and tools for metabolite profiling [105]. Panorama is a cloud-based platform that offers data analysis and visualization tools for collaborative plant omics research [106,107]. Genome editing technology utilizes specific enzymes to induce targeted genetic alterations by creating DNA double-strand breaks [108], including meganucleases (MNs), zinc-finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), and the CRISPR/Cas9 system [109]. MNs are naturally occurring enzymes that recognize long DNA targets (12–40 base pairs) and are encoded by introns or mobile genomic elements [110]. ZFNs and TALENs are engineered nucleases; ZFNs consist of a zinc-finger protein that binds DNA and a FokI endonuclease domain [111], while TALENs have a DNA-binding TALE domain and a FokI cleavage domain [112]. CRISPR/Cas9-mediated gene editing is revolutionizing the development of abiotic stress-tolerant crops. This technology allows targeted mutagenesis, gene knockouts, alterations, activation, and repression in various agricultural plants, including cereals, enhancing the ability of plants to withstand adverse environmental conditions [113]. Compared to ZFNs and TALENs, the CRISPR/Cas9 system is more cost-effective, efficient, and adaptable, making it the preferred genetic engineering strategy for creating superior crop varieties with improved yields under biotic or abiotic stress [114–117]. Data conversion into quantifiable measurements, computational analysis, and trait identification are the steps through which multi-dimensional crop traits from cellular to field levels are systematically acquired and analyzed by plant phenomics [118–121]. Crop production faces significant challenges due to abiotic stresses such as drought, salinity, and nutrient deficiencies, necessitating stress resistance phenotyping [122]. Ground-based platforms equipped with thermometer sensors and RGB cameras can be used to evaluate drought stress, while unmanned aerial vehicles with thermal cameras allow for rapid scanning of larger areas to identify resistant genotypes [123]. Salinity stress, impacting stomatal conductance, can be detected using visible to near-infrared spectral reflectance images and tools such as Scanalyzer3D to study tolerance mechanisms. Assessing tissue ion concentrations using RGB, fluorescence imaging, and hyperspectral imaging combined with ML can determine salinity tolerance [20,124]. Nitrogen deficiencies, which impact chlorophyll content, growth, and disease susceptibility in crops, are monitored using RGB, multispectral, and hyperspectral sensors. Mobile platforms integrating these sensors are used to efficiently estimate N content [125,126].

4. AI-Assisted Techniques for Abiotic Stress Management and Applications of AI in Crop Stress Biology

AI and ML are revolutionizing plant research and crop resilience and addressing agricultural/food security challenges [120]. Deep learning (DL), a machine learning specialization, trains artificial neural networks (ANNs), mimicking the brain's layered structure for automatic feature extraction [121]. Self-supervised DL models such as ESM-2, DNABERT-2, and MSA Transformer can extract novel insights on protein/DNA structure, function, and evolution without labeled data [122]. ESM-2 self-learns protein sequence properties by masking and predicting masked regions [123], and NetGO3 uses ESM for state-of-the-art gene ontology prediction from sequences [124]. The initial ML phase involves data collection, e.g., RNA sequencing (Figure 2) [20], and de-noising enhances expression recovery. Supervised ML uses diverse features such as amino acid sequences and physicochemical properties for training data representation [41]. Feature selection is crucial, with three methods: filter, wrapper, and embedding [42,43,127]. Algorithm selection is fundamental in ML, categorized into supervised (establishing input–output relationships from training data), unsupervised (identifying data patterns without known outcomes, e.g., clustering and dimension reduction) [128,129], and semi-supervised (handling labeled and unlabeled data) [130]. Common supervised algorithms include Support Vector Machine (SVM), Decision Tree (DT), Random Forest (RF), Artificial Neural Network (ANN), and Naïve Bayes (NB) [131], while k-means, ICA, and hierarchical clustering are unsupervised [132]. PCA reduces high-dimensional data to fewer uncorrelated PCs [133,134]. AlphaFold2 and conformational subsampling provide structural insights into plant stress protein interactions [135]. The latest work enables ab initio 3D ligand structure prediction in proteins for de novo molecule design [136]. AI advances include protein design via diffusion models [137] and protein interaction prediction driven by high-throughput data, hardware, and powerful methods [138]. However, AI techniques, including machine learning models such as SVM and neural networks, often demand significant expertise in algorithm development and data science. For beginners, AI platforms with pre-built models and intuitive interfaces, such as DeepAProt and ASRpro, offer a more accessible entry point into AI applications, although these may not provide the flexibility required for fully customized analyses.



	X_1	X_1	...	X_n	Y
1	X_1^1	X_2^1	...	X_n^1	Y_1
2	X_1^2	X_1^2	...	X_n^2	Y_2
...	...	...	...	...	...
m-1	X_1^{m-}	X_2^{m-}	...	X_n^{m-}	$Y_?$
m	X_1^m	X_2^m	...	X_n^m	$Y_?$

Figure 2. Fundamental steps in developing machine learning models (**A**). Types of machine learning: supervised (**B**) and unsupervised methods (**C**) [19].

5. Major Deep Learning Architectures

Machine learning is widely popular, with DL and ANN architectures gaining attention. Deep learning autonomously processes raw data, identifying complex patterns without requiring extensive domain knowledge, in contrast to traditional ML, which focuses on discrete or continuous output predictions [139]. Artificial Neural Networks (ANNs) imitate biological neurons, learning through synaptic connections [140]. Deep Neural Networks (DNNs) have numerous hidden layers, Recurrent Neural Networks (RNNs) handle sequential data [141], Convolutional Neural Networks (CNNs) identify features without supervision [142], and Graph Convolutional Networks (GCNs) tackle complex problems [143]. Transformers with self-attention are used for natural language tasks [144]. Ensemble classifiers combine multiple models [145]. Clustering methods such as k-means provide unsupervised protein function prediction [146,147]. Understanding each algorithm's strengths and/or weaknesses is crucial before applying them to omics datasets.

6. Validation of ML Predictions in Crop Genomics

Machine learning predictions can be validated in plant genomics through cross-validation and algorithm comparison. K-fold cross-validation involves randomly dividing the training data into k subsets, using one for validation and the others for training [148,149]. Evaluation metrics derived from the confusion matrix include sensitivity, specificity, accuracy, precision, F1-score, and MCC [150]. The ROC curve, which plots the False Positive Rate against the True Positive Rate, and the Area Under the Curve are used to measure performance, with a higher AUC indicating better prediction accuracy [151]. Individual-based models require context-oriented validation due to complex interaction structures [152,153], which involves visual inspection, statistical comparison, expert input, and experimental validation [154]. Pattern-oriented modeling verifies and validates functional-structural plant models [155]. Ontology-based approaches ensure model accuracy [156]. O2PLS integrates transcript and metabolite data for validation [157]. For plant omics ML models, context specificity is crucial for improving agronomic traits and crop resilience. ML is necessary for pathogen effector gene analysis and for integrating multi-omics data to reconstruct networks [158]. ML prediction validation in plant stress omics involves comparing classical and ML phenotype predictions [159], enhancing interpretability by classifying visual stress symptoms [160], standardizing assessments, and using imaging and ML for data assimilation [161].

7. Why Is Machine Learning Preferred for Analyzing Plant-Omics Data over Traditional Methods?

Machine learning, especially deep learning, is preferred over traditional methods for analyzing large, complex plant omics data from high-throughput sequencing [162,163]. Unsupervised and semi-supervised machine learning algorithms accurately analyze plant traits affected by genotype–environment interactions without requiring large, labeled datasets [147,158]. Decision tree ensembles excel at genomic prediction and integrative omics analysis [164–166], deciphering complex interactions such as pathogen effectors and plant immunity [167]. In transcriptomics, ML enhances differentially expressed gene identification [155], although non-linear models may need explainable AI for interpretation [167]. Integrating ML with biological knowledge aids in learning dynamics from large datasets [168–170]. ML's multivariate analysis proficiency enables biomarker discovery and predictive modeling [171]. While integrating multi-omics data remains challenging due to scaling issues [172], ML excels at feature selection, as shown in rice salt stress analysis using PCA and LASSO [173]. ML allows phenotype forecasting, biomarker identification, pattern recognition in complex datasets, and scalability for large-scale omics, driving its adoption due to its ability to address data intricacies, enable predictive modeling, facilitate exploratory analysis, and adapt to heterogeneous data [20]. In multi-omics analysis, Gene Regulatory Network (GRN) construction is a primary goal. With limited ChIP-seq data for transcription factor binding sites in plants, GRN inference heavily relies on expression data [174]. Traditional correlation and mutual information methods struggle with regulatory direction and temporal delays [175,176]. Probabilistic graphical models such as GENIST and JRmGRN improve this but require high spatiotemporal resolution [177,178]. Machine learning has revolutionized GRN inference by integrating multi-omics data [179,180]. Tools such as iDREM use hidden Markov models to reconstruct temporal GRNs from transcriptomic, proteomic, and epigenomic data [181]. For single-cell RNA-Seq, GRNBoost2 and SCENIC enable cell-specific GRN inference efficiently [182,183]. ML's strengths in handling complex data, integrating diverse datasets, predictive modeling, and exploratory analysis drive its adoption in plant omics [184].

8. AI Applications in Plant and Crop Omics for Combating Abiotic Stress

AI techniques, including ML and DL, are used to develop predictive models that can simulate crop responses to various stress conditions. These models assist in identifying key stress tolerance traits and optimizing breeding programs for stress-resistant crops [185]. AI-assisted omics techniques in plant defense research represent a state-of-the-art approach that merges advanced molecular technologies with AI to gain deeper insights into plant responses to stressors (Figure 3). These techniques enable the rapid identification of key components in defense pathways, the discovery of biomarkers, and the detection of hidden patterns, enhancing our understanding of plant defense mechanisms. By integrating multi-omics data sources, these methods provide a comprehensive perspective [186]. Machine learning algorithms are crucial in identifying stress resistance genes, which aids in plant and crop improvement. For instance, Liang et al. [187] employed an SVM variant to identify key genes in *A. thaliana* for drought resistance, while Shikha et al. [188] explained the superiority of Bayes algorithms in identifying critical SNPs in maize. Furthermore, Wang et al. [189] applied an SVM-based model to predict salt resistance genes in rice, whereas Ravari et al. [190] used artificial neural networks to identify indices to predict salt-tolerant varieties of Iranian wheat. Schwarz et al. [191] investigated the cis-regulatory code governing iron deficiency response in *Arabidopsis* roots using ML. For plant disease resistance, SVM variants have shown high accuracy in predicting resistance proteins [192].

Machine learning also aids in predicting pathogen effector proteins, with EFFECTORP being the first ML classifier for fungal effectors [193]. Despite the primary focus on resistance genes, ML also shows promise in understanding susceptibility genes, significantly impacting agricultural practices [194]. Opportunities to uncover cellular heterogeneity, decode regulatory networks, and identify novel cell types arise from applying ML to plant single-cell genomic data [166,195]. Methods such as SIMLR [196] and neural networks [197] address challenges in single-cell RNA sequencing, providing reliable insights.

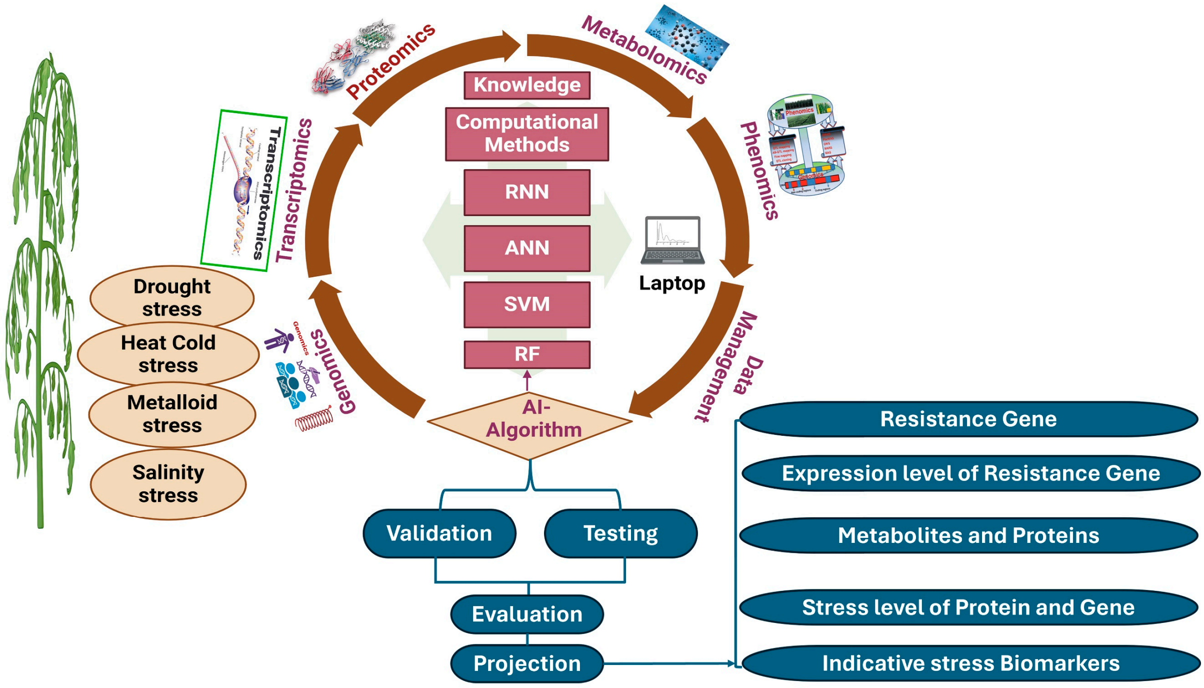


Figure 3. An integrated Omics and computational workflow for identifying and validating stress resistance genes and biomarkers in crops.

Studies on miRNAs and lncRNAs have demonstrated their regulatory roles in stress tolerance. Bioinformatics tools analyze the interactions between these RNAs and their target genes, providing insights into stress adaptation mechanisms [198]. Regarding exploring individual miRNA roles in *A. thaliana* plant stress responses, Asefpour Vakilian [199] employed feature selection algorithms, where information theory-based feature selection identified key miRNAs (miR-159, miR-169, miR-393, and miR-396) as significant contributors. Meng et al. [200] used supervised classification models to identify low-temperature SRGs in plants. Interestingly, models trained solely on genome assembly features showed only modest performance reductions compared to those using a wider range of data. Although models trained on one plant species successfully predicted cold stress gene responses in related species, multi-species models outperformed them in cross-species prediction accuracy. Zhou et al. [93] found extensive transcript abundance changes in maize genotypes subjected to high- or low-temperature stress through transcriptome profiling. Motifs near SRGs' transcription start sites (TSSs) were enriched. Predictive models leveraging these motifs were able to predict gene expression responses, with increased accuracy, particularly when focusing on un-methylated TSS-proximal motifs. Pradhan et al. [201] employed ML to identify long non-coding RNAs related to abiotic stress responses in plants, crucial for developing crop cultivars that are stress-resistant. They devised a computational model for binary classification to predict stress-responsive lncRNAs using stress-responsive and non-responsive lncRNA sequences (68.84% cross-validation accuracy and 76.23% accuracy on an independent test set was achieved). An online prediction tool, ASLncR, was also introduced. Similarly, Meher et al. [202] developed an ML-based method for predicting abiotic stress-responsive miRNAs and pre-miRNAs; using pseudo-K-tuple features and SVM, the model achieved auROC/auPRC percentages of 65.64–77.94% and independent test set accuracies of 62.33–69.21% across miRNA, pre-miRNA, and combined datasets. An online prediction server, ASRmiRNA, was provided to facilitate the identification of stress-responsive pre-miRNAs and miRNAs. Both studies leveraged machine learning, particularly SVM with nucleotide composition features, to accurately predict abiotic stress-responsive miRNAs and pre-miRNAs, enabling the development of stress-resistant crops. Online prediction servers were made available to improve accessibility. Ahmed et al. [203] introduced a new activation function in a DL model, i.e., Gaussian Error Linear Unit with Sigmoid (SIELU), designed to classify unknown abiotic stress protein sequences, achieving superior accuracies between 80.78% and 95.11%. In another study, Liu et al. [204] focused on classifying 216 plant species based on incomplete metabolite content. Their research made use of a network clustering algorithm to group structurally similar metabolites. Despite the incomplete data, this approach highlighted the importance of metabolite content as a taxonomic marker by successfully clustering plants according to known evolutionary relationships.

Deep learning techniques have demonstrated significant effectiveness in managing various plants and crops. For instance, a study on plant defense against salinity stress [205,206] employed image processing and DL algorithms. This study incorporated high-throughput plant phenotyping technologies, hyperspectral imaging (HSI), and advanced techniques for segmenting plants and leaves. Table 2 provides an overview of ML-based tools specifically designed to tackle abiotic stress in plants. These specialized tools address specific stressors, offering valuable resources for researchers and practitioners focused on plant defense. PCA and hierarchical clustering are employed for data visualization and gene expression pattern analysis [207–209]. Algorithms such as t-SNE, OPTICS, and NMF aid genotypic data analysis and metagene identification [210,211]. Transfer learning predicts specialized metabolism genes in tomatoes using *Arabidopsis* data to address limited annotated plant data [212]. 'Evolutionarily informed ML' uses *Arabidopsis* transcriptomics to predict maize plant's N-use efficiency genes [213]. For single-cell sequencing's high dimensionality, advanced algorithms such as t-SNE, UMAP, PHATE, MAGIC, Beeline, and Saucie are employed in plant and human studies [214–218].

Table 2. AI-driven tools for enhancing plant defense against abiotic stress [20].

Tools	Abiotic Stressor	Algorithm	Features and Description	Websites
ASRpro	Drought, salinity, light, high and low temperatures	SVM	Autocross covariance and K-aner composition identification of proteins.	https://iasri-sg.icar.gov.in/asrpro/ (accessed on 1 March 2024)
AsmIR	Drought, salinity, high and low temperatures	SVM	Pseudo-K-tuple nucleotide composition; predicts abiotic stress miRNA.	https://iasri-sg.icar.gov.in/asmir/ (accessed on 1 March 2024)
PlncPRO	Abiotic	RF	Predicts abiotic stress-responsive long non-coding RNA	http://ccbb.jnu.ac.in/plncpro/ (accessed on 1 March 2024)
ASRmiRNA	Abiotic	SVM	Predicts abiotic responsive miRNA.	http://cabgrid.res.in:8080/asrmirna/dataset.html (accessed on 1 March 2024)
ASLncR	Abiotic	SVM	Predicts abiotic stress-responsive long non-coding RNA.	https://iasri-sg.icar.gov.in/aslncr/ (accessed on 1 March 2024)
Ir-HSP	High temperatures	SVM	Categorizes protein sequences into one of the heat-shock families	http://cabgrid.res.in:8080/ir-hsp/ (accessed on 1 March 2024)
DeeperHSP	High temperatures	CNN	Identifies heat-shock proteins.	https://github.com/seonwoo-min/DeeperHSP (accessed on 1 March 2024)
AFP-Pred	Cold	RF	Predicts anti-freeze protein properties.	https://www3.ntu.edu.sg/home/EPNSugan/index_files/AFP-Pred.htm (accessed on 1 March 2024)

9. Challenges in Bioinformatics Education and AI for Crop Improvement under Abiotic Stress

The transformative impact of 'Next-Generation Sequencing' technologies on genomics research is evident, rendering it more cost-effective and efficient. However, the burgeoning complexity of data poses a significant challenge, with data analysis emerging as the primary bottleneck. Regardless of the availability of numerous genome assembly tools, de novo genome assembly employing NGS data encounters formidable obstacles such as sequencing errors, bias, repetitive regions, and substantial computational resource requirements [219]. The accuracy of sequencing data assumes paramount importance for subsequent analysis. Hence, the development of user-friendly bioinformatics platforms is imperative for analyzing vast multi-omics datasets generated by high-throughput technologies. Collaborative data-sharing initiatives and adherence to common data standards facilitate the effective utilization of bioinformatics resources. The integration of AI and ML with omics data holds considerable promise, although it does face challenges. Each ML algorithm exhibits specific strengths and weaknesses that influence predictive efficiency. Omics datasets are inherently noisy and sparse, posing challenges in accurately identifying biological features when integrating diverse sources [220]. Addressing imbalanced datasets is a prevalent issue, often tackled through resampling strategies such as SMOTE [221,222]. Overfitting poses a threat to the predictive capabilities of deep learning models, but techniques such as dropout offer mitigation [223]. Factors such as data pre-processing, parameters, and domain knowledge significantly influence ML effectiveness, necessitating adaptability to multi-omics data and high dimensionality. The interpretation of complex models remains a formidable challenge.

AI-assisted omics techniques hold the potential to revolutionize plant research and agriculture. They facilitate early disease detection by analyzing molecular profiles before visible symptoms appear, real-time plant health monitoring by correlating omics data with phenotypes, prediction of disease dynamics by modeling genetic and environmental factors, and customization of plant breeding for disease resistance. Moreover, AI can optimize sustainable disease management by integrating omics data for precise pesticide application. Future research endeavors should prioritize understanding plant responses to combined biotic and abiotic stressors. The integration of AI-assisted omics with remote sensing presents a potent approach to monitoring and mitigating plant stress. However, the practical implementation of AI in plant omics necessitates robust algorithms, experimental validation, and fostering collaborative connections among researchers, agricultural experts, and data scientists. Additionally, the economic feasibility of integrating drone technology into crop research underscores the potential for substantial returns on investment, driven by improved crop monitoring and optimized resource use. In the context of managing abiotic stress, drones offer a significant advantage by enabling precise and timely responses to environmental challenges, which is critical for crops under stress conditions. While the initial investment can vary significantly, the potential for substantial returns on investment exists when drones are effectively used to optimize resources such as water, fertilizers, and pesticides [224]. This economic feasibility is crucial for scaling AI-driven stress management solutions, as it allows for more precise interventions compared to traditional methods such as manual scouting or satellite imagery, especially under variable weather conditions [225]. Education in relevant technologies and bioinformatics assumes critical importance in accurately translating experimental efforts. AI-based solutions such as genetic algorithm-based 'Internet of Precision Agricultural Things' are gaining momentum for real-time problem-solving in agriculture, such as predicting water requirements [226] and aiding decision-making on plant patterns and water management. Integrating multi-omics data, big data technology, AI, and robust bioinformatics analysis through approaches such as "integrated genomic-environs prediction" can expedite plant breeding programs and enhance genetic gains [227]. Establishing integrative plant breeding platforms and open-source initiatives can catalyze smarter plant breeding endeavors.

10. Conclusions

The convergence of bioinformatics tools and artificial intelligence offers a transformative approach to managing abiotic stress in plants. By integrating multi-omics data and leveraging advanced AI algorithms, scientists can garner profound insights into the complex regulatory networks and molecular mechanisms underlying stress responses. Bioinformatics tools facilitate the identification of stress-responsive genes, regulatory elements, and molecular markers, while AI techniques enhance predictive modeling, gene regulatory network interference, and real-time plant monitoring. These innovations are critical for developing stress-resilient plant varieties capable of thriving in increasingly harsh environmental conditions due to global climate change and anthropogenic activities. Practical applications include predicting drought-resistant gene variants, identifying salt-tolerant crop varieties, and real-time monitoring of plant health under extreme temperature conditions through AI-driven phenomics platforms. AI and bioinformatics education can also solve other agricultural problems, such as predictive modeling for disease management, optimizing resource use, genetic improvement, enhanced crop monitoring, automated farming systems, and climate adaptation. For instance, AI can analyze large datasets to predict plant disease outbreaks, optimize water and fertilizer use, identify genetic markers for plant improvement, and model climate change scenarios to help farmers adapt their practices. These technologies also facilitate real-time monitoring and automation in farming, increasing efficiency and reducing labor costs. Despite the remarkable progress, several challenges remain there. Developing user-friendly bioinformatics educational platforms, establishing common data standards and addressing issues such as overfitting, data imbalance, and model interpretability are essential for the effective integration of AI and omics data. Recognizing the diverse needs of researchers, from novices to experts, our review emphasizes the importance of selecting tools that match the user's proficiency level. Educational initiatives, interdisciplinary collaborations and trainings are essential to equip the next generation of researchers with the required skills to utilize these advanced tools effectively. By fostering a collaborative environment, the scientific community can drive innovation and address global food security challenges more effectively. Integrating AI and bioinformatics education creates a robust framework for enhancing abiotic stress tolerance in plants and crops, offering a holistic strategy that is crucial for advancing sustainable agriculture, securing food supply, and mitigating the impacts of climate change on global crop production.

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