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Turbocharging crop breeding with integrated biotechnology for a climate-resilient future[FA]

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ABSTRACT

Global agriculture faces unprecedented challenges from climate change and population growth, creating an urgent demand for the rapid development of resilient and high-yielding crop varieties. Although conventional breeding has achieved substantial progress in crop improvement, it is increasingly constrained by bottlenecks in genetic diversity, efficiency, and the uncertainty of trait inheritance under complex environments. Recent advances in integrative biotechnology offer transformative opportunities to reconfigure crop improvement into a predictive and design-driven process. This review synthesizes these advances into an integrated, multidisciplinary framework for precise breeding of climate-resilient crops, emphasizing the need to move beyond descriptive data accumulation toward mechanistic integration and beyond single-trait modification toward systems-level design. By integrating genome-phenome-environment insights with artificial intelligence-powered predictive modeling, we envision the rise of precise breeding frameworks capable of rapidly delivering climate-resilient, high-yielding crops. Such approaches are critical to fortifying agricultural systems, mitigating climate vulnerability, and securing a sustainable food future.

Keywords: artificial intelligence, climate-resilient crops, precision breeding, sustainable agriculture

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INTRODUCTION

Global agriculture is entering a period of unprecedented pressure as population growth and climate change converge. The Food and Agriculture Organization of the United Nations (FAO) projects that the world population will reach nearly 10 billion by 2050, thus requiring at least a 60% increase in food production to meet global demand (Figure 1; Hickey et al., 2019; Lu et al., 2025). Yet this goal is being critically undermined by climate change. Increasingly frequent extreme weather events such as heat waves, droughts, soil salinization, and flooding are already eroding both the yield and quality of staple crops, casting serious doubt on the capacity of current agricultural systems to sustain future food security (Lobell et al., 2011; Ceccarelli and Grando, 2020; Cooper et al., 2021; Langridge et al., 2021; Hafeez et al., 2023). For example, global crop yields are estimated to decline by 3%–7% with every 1°C rise in temperature (Zhao et al., 2017). Between 1983 and 2009, nearly three-quarters of major crops experienced yield losses due to drought, highlighting the pervasive impact of extreme events. Over recent decades, climate change has already eroded agricultural productivity, offsetting the equivalent of roughly 7 years of technology-driven yield gains (Zhao et al., 2017; Ortiz-Bobea et al., 2021). Beyond single stress factors, crops in the field increasingly confront compound and

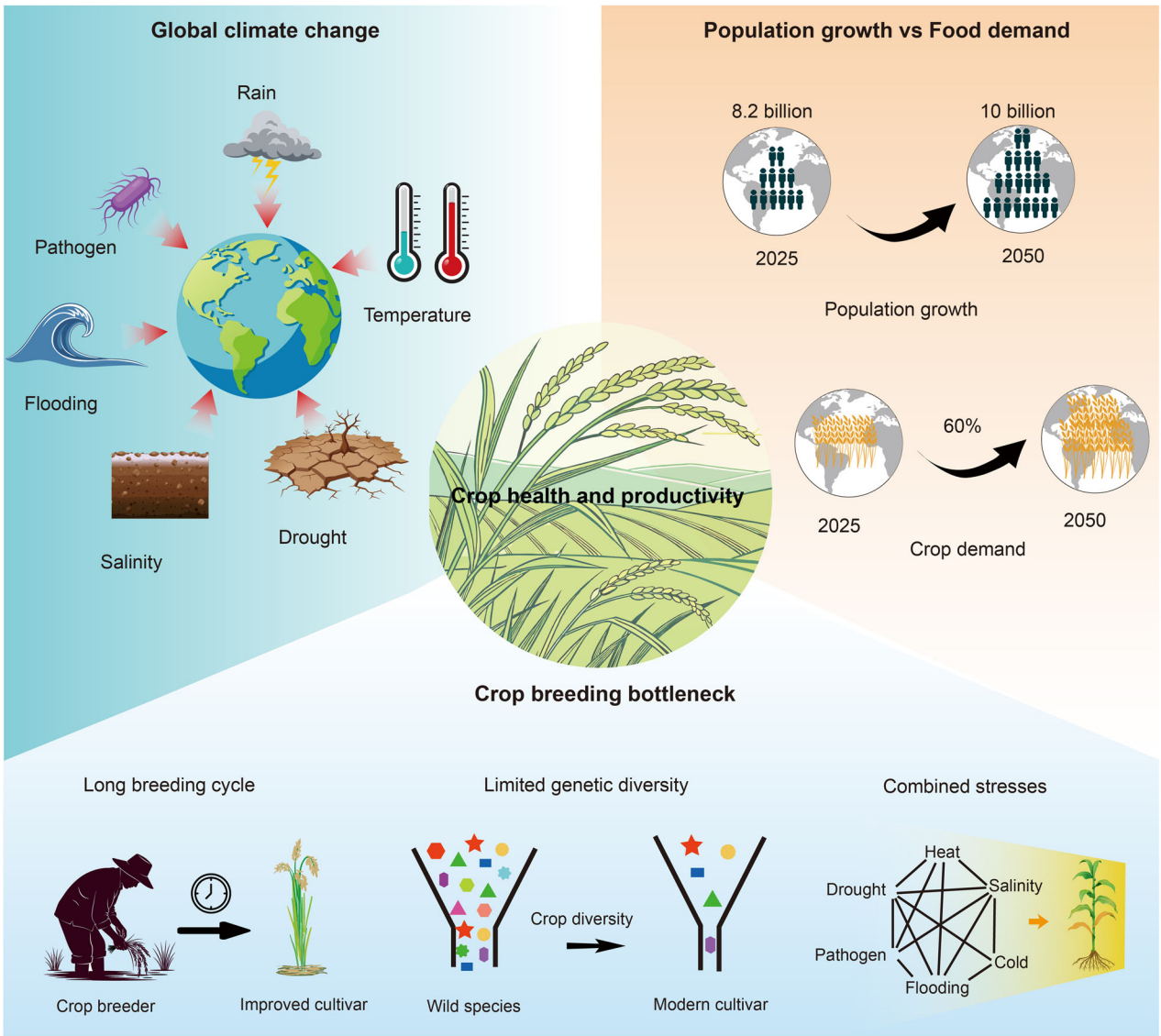

Figure 1. Crop breeding bottlenecks amid climate change and food demand pressures
Agricultural systems expose crops to combined abiotic stresses and biotic stresses, which compromise yield and quality. Projected global population growth and the resulting increase in food demand by 2050 underscore the pressing need for high-yielding and stress-resilient crop cultivars. Current crop breeding faces these core bottlenecks: long breeding cycles, reduced genetic diversity of cultivated varieties, and the technical complexity in breeding for combined stress resistance. There is an urgent need to address breeding limitations to mitigate the risks facing global food security.

sequential stresses; for example, drought and heat followed by intense rainfall and pathogen outbreaks, which amplify damage beyond the additive effects of single stresses (Zhou et al., 2017; Li et al., 2025). Such stress combinations do not follow a simple additive pattern; rather, they trigger nonlinear, amplified reductions in crop productivity (Figure 1; Pascual et al., 2022; Renziehausen et al., 2024). Together, these challenges crystallize a central demand in crop improvement: ensuring yield maximization under optimal conditions while safeguarding productivity under stress. Against this backdrop, developing climate-resilient crops with broad environmental adaptability has become a cornerstone for ensuring global food security (Springmann et al., 2018; Hickey et al., 2019).

Climate resilience refers to the capacity of crops to sense and adjust to changing conditions, thereby maintaining stable yields under complex, dynamic, and often unpredictable environments (Hill and Mackay, 2004; Walker et al., 2004; Farooq et al., 2024). Achieving this goal, however, has always depended on the tools of plant breeding. The history of crop improvement stretches back to the earliest stages of plant domestication, when humans relied on keen observation and artificial selection to fix advantageous traits such as higher yield or disease tolerance. This primitive form of breeding was slow and inefficient. It often took millennia to fix single traits, as evidenced by the gradual domestication of staple crops such as rice and wheat

(Tanno and Willcox, 2006; Fuller et al., 2009; Wang et al., 2018a; Ahmar et al., 2020). The emergence of hybrid breeding, sometimes described as the "second generation" of crop improvement, marked a turning point by grounding selection in the principles of genetics. This approach reduced the trial-and-error nature of domestication, allowing breeders to more deliberately target favorable traits (Wallace et al., 2018). Advances in genetics and biostatistics further expanded the scope of hybrid breeding, enabling the use of broader genetic resources and more systematic strategies. Yet important limitations remain: Breeding outcomes can be highly stochastic, reliance on narrow parental pools reduces genetic diversity, and multi-gene traits such as stress tolerance and yield stability remain difficult to capture due to linkage drag and polygenic complexity (Meyer and Purugganan, 2013; Wallace et al., 2018).

Of greater concern, conventional breeding has largely relied on the assumption of relatively stable selection environments; for instance, screening for drought tolerance in consistently arid regions or salinity tolerance in coastal zones. Climate change is intensifying both the severity and temporal clustering of extremes, raising the likelihood of these multifactorial events across major breadbaskets. Such stress combinations produce distinct physiological and molecular states (impaired photosynthesis, hormone imbalance, weakened immunity) that reduce recovery capacity and drive disproportionate yield loss, yet remain poorly represented in breeding targets and experimental screens (Rapport and Whitford, 1999; Zandalinas et al., 2021; Lesk et al., 2022; Pascual et al., 2022). Compounding the challenge, traits associated with climate resilience are typically governed by complex regulatory networks and exhibit strong genotype-by-environment interactions. Their expression varies markedly across locations and cultivation conditions, complicating breeding decisions and inflating resource requirements. Even genes that confer stress tolerance under controlled experimental conditions often fail to deliver consistent benefits in farmers' fields, where performance is disrupted by environmental fluctuations, background dependence, or regulatory trade-offs. Compounding these limitations, modern crop improvement has been accompanied by a progressive erosion of genetic diversity, driven by intensive selection within narrow elite germplasm pools. Although such strategies have delivered short-term yield gains, they have promoted breeding homogenization and the widespread deployment of closely related cultivars, increasing systemic vulnerability to novel and compound stresses. Extensive phenotypic and genomic selection within restricted genetic pools often yields diminishing returns, recycling redundant allelic variation while reinforcing genetic bottlenecks that constrain further yield improvement (Fu, 2015; Sun et al., 2024). Consequently, many traits critical for climate resilience, such as tolerance to fluctuating water availability, thermal instability, or combined abiotic–biotic pressures, are rare or absent in modern cultivars but persist in landraces, wild relatives, and underutilized species shaped by heterogeneous environments (Warschefsky et al., 2014). Continued reliance on existing crop gene pools therefore risks reinforcing yield ceilings rather than overcoming them, underscoring the need to broaden crop genetic diversity to sustain future gains under climate change. Together, these challenges expose the bottlenecks and limits of conventional breeding in addressing the demands of climate resilience. They underscore the urgent need for next-generation breeding strategies that integrate mechanistic understanding with systems-level design, offering a more predictive and effective path toward developing crops capable of withstanding the uncertainties of a changing climate. Modern biotechnologies are opening unprecedented opportunities for crop improvement through precision breeding approaches such as genomic selection, genome editing, epigenetic regulation, multi-omics integration, and artificial intelligence-assisted design (Gosal et al., 2010; Niazian and Niedbała, 2020; Steinwand and Ronald, 2020). These advances not only enhance our ability to dissect the genetic basis of complex traits such as drought tolerance, heat stability, and yield resilience, but also accelerate the precise identification and rapid assembly of favorable alleles. Against the dual backdrop of agricultural transformation and the climate crisis, a central challenge lies in integrating these diverse technologies into a forward-looking framework for intelligent breeding of climate-resilient crops. This review synthesizes recent progress in biotechnology-driven breeding, examines critical technical and translational bottlenecks, and proposes strategies for multi-stress adaptation, with the goal of providing conceptual and technological pathways toward faster and more precise genetic improvement.

To address the fundamental limitations of conventional breeding concerning efficiency, precision, and environmental adaptability, modern biotechnology is converging into an integrated, multidisciplinary framework for intelligent crop breeding. In this review, we outline four major pathways that represent current breakthroughs in modern breeding technologies: (i) accelerating genetic gain through shortened breeding cycles; (ii) high-throughput precision creation of breeding-ready stress-resilience modules; (iii) engineering climate resilience via design-driven strategies; and (iv) converging disciplines to power next-generation breeding (Table 1).

ACCELERATING BREEDING CYCLES FOR CLIMATE-RESILIENT CROPS IMPROVEMENT

Conventional hybrid breeding necessitates significant time and labor investment, often requiring three to 5 years or even decades to release a commercial cultivar (Labroo et al., 2021). This prolonged breeding cycle is unable to meet the urgent demand for new varieties under rapidly changing environmental conditions, and has become one of the major bottlenecks in plant research and crop breeding. On the one

Table 1. Core strategies and technologies for climate-resilient crop breeding.

Strategy	Key technologies
Accelerating breeding cycles	Doubled haploid
	Speed breeding
	Genomic selection
	Meiotic crossover
Precision identification of stress-related genes	Genomic mapping and structural variation
	Transcriptomic
	Proteomics and metabolomics
	High-throughput phenomics
	Integrative multi-omics strategies
Design-driven strategies	Precision editing
	De novo domestication
	Rational design of genetic networks and synthetic modules
Interdisciplinary approaches empowering biotechnology	Chemistry and physics technologies
	AI and robotics

hand, shortening the plant growth cycle and generation turnover can markedly accelerate the pace of breeding iterations, thereby enabling the selection and fixation of target traits within a much shorter timeframe (Samantara et al., 2022). On the other hand, comprehensive exploration and utilization of wild germplasm resources provide a gene pool of genetic diversity for the development of new varieties with enhanced environmental adaptability (Salgotra and Chauhan, 2023). It is noteworthy that the core of acceleration lies not only in the optimization of technological pathways but also in the acquisition and utilization of elite germplasm resources. How to collect and conserve seed resources more scientifically and systematically on a global scale, and how to employ modern biotechnological approaches to achieve precise evaluation and efficient utilization of their genetic potential, have become critical steps that determine the effectiveness of future breeding efforts. Therefore, the integration of accelerated growth cycles with efficient utilization of genetic resources not only opens new avenues for the rapid development of climate-resilient crops but also establishes a solid foundation for high-throughput and efficient molecular design breeding, carrying significant strategic implications for promoting sustainable agriculture and global food security.

Doubled haploid for rapid homozygosity

One of the most widely adopted approaches is doubled haploid (DH) technology, which enables the rapid production of completely homozygous lines within only two or three generations, in contrast to the multiple cycles of selfing required in conventional schemes (Germana, 2011; Meng et al., 2022). The process fundamentally relies on the use of haploid cells and the induction of chromosome doubling through either natural or artificial methods to rapidly generate homozygous diploid plants (Germana, 2011). It is particularly useful for developing genetic analysis materials and rapidly stabilizing superior recombinant genotypes (Figure 2A). The application of DH has become routine in major crops such as maize, wheat, and rice, where standardized pipelines now support both research and commercial breeding (Prasanna et al., 2012). The integration of highly efficient haploid inducer lines and automated screening methods has further expanded the scalability of this approach. For instance, the utilization of identifiable traits, such as color markers and high oil content, facilitates mechanized haploid seed identification, thereby greatly enhancing operational efficiency and accuracy (Song et al., 2017; Qu et al., 2021). In rice, Liu et al. successfully developed an efficient haploid induction line, HI285, and combined it with photo-thermo-sensitive genic male sterile (PTGMS) lines to establish a practical, high-throughput haploid production platform (Liu et al., 2024a). This breakthrough not only accelerated line fixation but also facilitated the large-scale application of DH in rice breeding. In maize, conventional hybrid breeding in maize requires up to eight generations of repeated selfing or backcrossing to stabilize the target genetic background, whereas DH technology enables the production of homozygous lines within two generations, significantly shortening the breeding timeline and enhancing breeding efficiency (Ren et al., 2017; Wang et al., 2019). In addition, breeders can induce a developmental fate switch in plant microspores through stress treatments such as high temperature or nutrient starvation, reprogramming the gametophytic pathway toward embryogenesis to produce doubled haploids (Germana, 2011). This strategy can substantially accelerate the development of inbred lines and cultivar improvement and has been successfully applied in crops such as rapeseed, tobacco, and wheat. However, in legumes and fruit trees, the low efficiency of regeneration systems necessitates specific stress treatments, and the process is strongly genotype-dependent, exhibits low induction efficiency, and is constrained by the developmental stage of microspores or pollen, which collectively limit its large-scale application (Croser et al., 2006; Weyen, 2021). Shi et al. found that under conventional stress treatments, the transcription factor BABY BOOM (BBM) is specifically induced in microspores (Shi et al., 2025a). Ectopic expression of *BBM* in tobacco and rice microspores can trigger fate reprogramming and embryogenesis even in the absence of stress. Further studies identified a novel BBM downstream effector, *BBM-activated androgenesis regulator 1* (*BAR1*), whose expression can independently initiate the embryogenic process in microspores, performing a cell fate reprogramming function similar to that of BBM. Through the BBM–BAR1 regulatory module, microspores can be directly redirected from the gametophytic developmental pathway to the embryogenic pathway, providing a theoretical basis for establishing an efficient, cross-species applicable doubled haploid induction

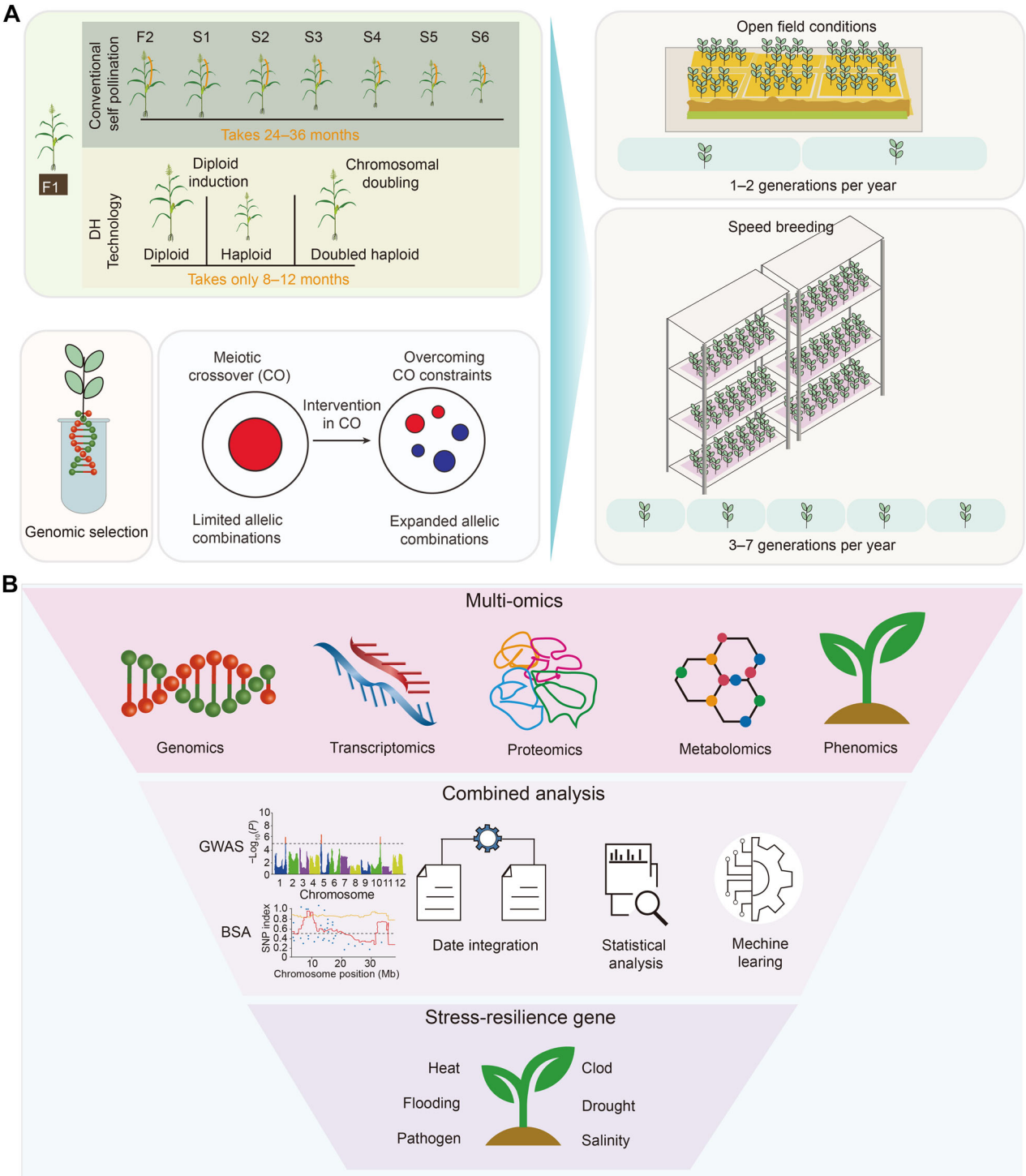

Figure 2. Accelerated breeding and precision identification of crop stress-resilience genes
(A) Strategies for accelerated crop breeding. **(B)** Multi-omics pipeline for crop stress-resilience gene identification.

system (Shi et al., 2025a). The development of DH technology now represents not only an improvement in breeding workflows but also an important driver of paradigm shifts in crop genetic improvement. With the continuous elucidation of the molecular mechanisms underlying haploid induction, the discovery of novel regulatory factors is expanding the boundaries of traditional approaches, enabling both cross-species applicability and high efficiency.

Speed breeding for rapid generation advancement

Under natural field conditions, most plants complete only one to two generations per year, which makes the conventional

genetic improvement process highly time-consuming and impedes a swift response to the escalating pressures of climate change. Speed breeding (SB) is another approach for rapidly developing new plant varieties (Potts et al., 2023). By exploiting controlled environment facilities, SB accelerates both vegetative growth and reproductive development by artificially controlling environmental conditions, including photoperiod, temperature, humidity, and CO_2 concentration, thereby shortening generation cycles and expediting genetic improvement (Ghosh et al., 2018; Watson et al., 2018; Figure 2A). Currently, SB has been effectively applied to various crops. For instance, it is utilized to accelerate the screening of traits associated with disease resilience in wheat (Alahmad et al., 2018; Ghosh et al., 2018). In soybean cultivation, adjusting the photoperiod and carbon dioxide concentration can shorten the growth cycle from 102–132 d to approximately 70 d, enabling the potential for up to five generations per year through rapid propagation (Nagatoshi and Fujita, 2018). Importantly, SB technology can be integrated with gene editing techniques to achieve targeted mutations and the rapid fixation of desired traits. In crops such as rapeseed, cabbage, and soybean, researchers have successfully generated edited seeds within a short timeframe using genome editing systems such as CRISPR/Cas9 (Yang et al., 2017; Murovec et al., 2018; Bao et al., 2020). This advancement significantly enhances the efficiency of target gene introgression and accelerates the pace of genetic improvement. However, the high cost of constructing and operating controlled-environment systems of SB remains a significant challenge, which consequently limits their adoption in certain developing countries and small to medium-sized breeding institutions (Samantara et al., 2022). Nevertheless, as a "time accelerator", rapid breeding technology demonstrates significant potential in overcoming the limitations of breeding cycles and is particularly well-suited for expediting the breeding process of crops that exhibit environmental adaptability.

Genomic selection for predictive breeding

Genomic selection (GS) improves breeding by constructing predictive models that associate genome-wide molecular marker genotypes with phenotypes in a training population, thereby guiding the selection and advancement of candidate lines (Sinha et al., 2023). These models are subsequently applied to predict the breeding values of untested individuals with known genotypes, thereby facilitating efficient and precise selection within breeding populations. Compared with conventional marker-assisted selection, GS does not require significance testing of markers (Collard and Mackill, 2008). It is particularly suitable for quantitative traits controlled by many minor-effect loci, enabling shorter breeding cycles and reducing breeding costs (Collard and Mackill, 2008). As a result, the practical utility of GS has been demonstrated in several crops. In rice, 278 individuals were randomly selected from 21,945 hybrid progenies derived from 210 recombinant inbred line parents for phenotypic evaluation. This set served as a training population to predict yield-related traits of all potential hybrids. The average yield of the top 100 hybrids showed a 16% increase compared with the average yield of all potential hybrids (Xu et al., 2014). The advancing development and application of GS present promising new avenues for crop breeding. Furthermore, when integrated with the precise identification of genes underlying key agronomic traits, GS can significantly accelerate the accumulation of favorable alleles and broaden the genetic variation available for cultivar improvement (Crossa et al., 2017).

Modulating meiotic recombination to expand genetic diversity for crop breeding

Within the framework of crop breeding, overcoming the constraints of meiotic crossover (CO) can greatly expand the spectrum of accessible allelic combinations and genetic variation (Fernandes et al., 2019). Increasing the overall recombination rate, altering the spatial and temporal distribution of crossovers, or inducing targeted recombination at specific loci can release long-suppressed variation, thereby enabling the incorporation of beneficial variants from wild relatives or rare alleles into the breeding pool and increasing the range of selectable phenotypic combinations (Choi, 2017). Establishing a closed loop from the elucidation of underlying mechanisms to the development of applicable recombination engineering strategies will provide a critical theoretical foundation and practical pathway for constructing broader and functionally controllable germplasm resources, enhancing population genetic diversity, and accelerating the breeding process. In eukaryotes, CO during meiosis is the central mechanism mediating the exchange of genetic material between homologous chromosomes, playing a decisive role in ensuring accurate segregation of chromosomes in gametes and maintaining population genetic diversity (Shang et al., 2022). The innovation of breeding materials largely depends on the creation of novel allele combinations. By aggregating favorable alleles and eliminating linked deleterious alleles, it is possible to develop breeding materials with improved traits. This process is typically constrained by the number of CO occurring during meiosis (Blary and Jenczewski, 2019). In addition, CO frequency and distribution often exhibit significant differences between male and female individuals, and the underlying molecular mechanisms remain unclear. In crop genetic improvement, large genomic regions are difficult to recombine effectively due to the limitations in CO number and distribution, posing a critical bottleneck for assembling favorable alleles and breaking undesirable linkages in precise breeding (Lloyd, 2023). Therefore, modifying CO distribution patterns holds significant importance for breeders. In response to these issues, research in recent years has gradually focused on enhancing recombination rates through genetic, molecular, and environmental intervention methods, with the aim of providing new solutions for precision breeding. Multiple studies have already identified the key factors and pathways that regulate meiotic recombination and explored feasible strategies to

increase CO frequency or alter its distribution pattern, thereby breaking genetic linkage and promoting the accumulation of favorable alleles (Kuo et al., 2021). The synaptonemal complex is a crucial structure that determines crossing over and chromosome segregation during meiosis. The *ZEP1* gene encodes a key component of the synaptonemal complex. CRISPR/Cas9-mediated creation of *zep1* mutants resulted in complete male sterility, whereas female fertility was largely unaffected. In these mutants, the frequency of genetic recombination was substantially increased, and CO interference was entirely abolished (Liu et al., 2021). In Arabidopsis, simultaneous mutation of *ZYP1* and *RECQ4* achieved an unprecedented increase in CO number, with the number of CO in female gametes rising by up to 12-fold and in male gametes by 4.5-fold. This substantial enhancement of recombination effectively disrupted large linked genomic regions, thereby facilitating the aggregation of favorable alleles. Further studies have introduced the concept of crossover potential (COP), which is determined by genomic features such as chromatin state and sequence homology and is highly consistent between female and male individuals. Although the ultimate distribution of CO remains regulated by factors including interference and sexual dimorphism, these findings indicate that targeted modulation of CO formation pathways can markedly increase recombination levels without substantially reducing fertility, thereby accelerating the generation and utilization of genetic diversity. This provides a novel molecular strategy and theoretical basis for breaking linkage barriers, minimizing introgressed segments, and improving breeding efficiency (Jing et al., 2025). In summary, targeted modulation of meiotic recombination pathways not only provides a novel molecular strategy for breaking linkage barriers and accelerating the aggregation of favorable alleles but also further expands the potential for generating genetic diversity (Figure 2A).

Overall, approaches such as DH, SB, and GS mainly focus on accelerating the improvement of existing crops. These strategies often generate synergistic effects when applied together; for example, the integration of DH and SB enables the rapid iteration of homozygous lines within an extremely short timeframe, thereby providing an efficient material basis for crop improvement. When these approaches are combined with the targeted modulation of meiotic recombination, the enhanced genetic diversity from recombination engineering, together with the acceleration of homozygosity by DH, the generational advancement enabled by SB, and the predictive power of GS, jointly establish a highly efficient breeding system. Recently, Xie et al. (2025) integrated genome editing with an artificial intelligence-based robot (GEAIR) system and speed breeding to accelerate the genetic improvement of tomato. By employing genome editing to rapidly reshape flowering time and plant architecture in wild tomato, they aligned growth rhythms with modern cultivars, thereby overcoming long-standing hybridization barriers caused by asynchronous flowering and dispersed plant structures between wild and cultivated tomatoes. Building on these advancements, researchers applied GEAIR in LED-controlled environments to implement high-throughput, multi-to-multi hybridization designs, substantially enhancing breeding efficiency and combination diversity. Concurrently, speed breeding extended the photoperiod and optimized temperature conditions, enabling populations to complete three to seven generations per year, which significantly reduced the time required for genetic improvement. These findings indicate that the deep integration of intelligent breeding platforms and speed breeding not only enables the reconstruction of genetic diversity within a relatively short timeframe but also facilitates the rapid aggregation and optimization of complex agronomic traits. More importantly, this approach provides a feasible pathway for establishing high-throughput, controllable, and intelligent breeding platforms, while offering a systematic and integrated solution to accelerate breeding, thereby demonstrating a new direction for future crop improvement (Figure 2A).

PRECISION HIGH-THROUGHPUT IDENTIFICATION OF STRESS-RESILIENCE GENES

Under increasingly complex and variable climatic conditions, the precise identification and deployment of stress resilience genes have become a central objective in molecular breeding. However, long-term selection focused on high yield has substantially reduced the genetic diversity of cultivated species, leading to the marginalization or loss of valuable stress resilience genes present in many wild relatives. This erosion of diversity has left modern crops lacking resilience and with limited capacity to respond to sudden environmental stresses (Brown, 2016). Overcoming this limitation requires a systematic framework for the identification of resilience-associated genes, thereby enabling the rational design of crops that can withstand multifactorial stress conditions. With the significant reduction in next-generation sequencing (NGS) costs, multi-omics integration strategies have increasingly become a vital support for breeding crops with environmental adaptability.

Genomic mapping and structural variation for stress-resilience gene identification

Linking genome variation identification with transcriptomic expression analysis, functional validation, and regulatory mechanism decoding allows researchers to construct an integrated framework of variation-expression-function (Satam et al., 2023; Kumar et al., 2024). This systems-level approach facilitates not only the discovery of key loci but also the unraveling of regulatory cascades that mediate complex stress responses. The majority of stress tolerance traits in plants are quantitative traits that are controlled by multiple genes and influenced by the interaction between environmental factors and genetic components (Andrade et al., 2020; Raj and Nadarajah, 2022). Identifying these loci

remains a cornerstone of stress genomics. Currently, two primary methods are widely used for quantitative trait locus (QTL) identification: linkage analysis and genome-wide association study (GWAS) (Hill and Mackay, 2004). In linkage analysis, biparental populations are developed from parents with contrasting phenotypes. This strategy is effective for reducing genetic background noise, but it can only detect two alleles at a given locus. During the construction of biparental populations for QTL analysis, the offspring undergo only a limited number of recombination events, which generally results in low mapping resolution (Bernacchi and Tanksley, 1997; Meuwissen and Goddard, 2004). In contrast, GWAS leverages natural populations, thereby avoiding the need for dedicated mapping populations. Unlike linkage analysis, which only considers two alleles at a locus from parental lines, GWAS can simultaneously detect multiple alleles at the same locus, thus enabling higher-resolution QTL mapping (Klein et al., 2005; Cantor et al., 2010; Manolio, 2010; Alseekh et al., 2021). Bulked Segregant Analysis (BSA) provides an efficient alternative for the rapid localization of loci associated with quantitative traits (Figure 2B). This method was first proposed by Michelmore, and its central concept is to select individuals with extreme phenotypes from a segregating population, pool their DNA into two contrasting bulks, and subsequently compare allele frequency differences between the bulks through high-throughput genotyping (Michelmore et al., 1991). BSA does not require the construction of a large-scale genetic linkage map, and its workflow is simplified while offering higher efficiency in locus identification. Moreover, it relies less on population size and enables precise localization of candidate genes within a broader genomic background (Takagi et al., 2013; Schneeberger, 2014), thereby providing a powerful tool for the rapid discovery of stress-resilience-related genes in plants under adverse conditions.

With the advancement of high-throughput sequencing technologies and population genomics, researchers have begun to leverage pan-genome construction and structural variation analysis to identify key genes associated with traits. These approaches can reveal genomic differences among varieties or populations, capture rare or specific variants that are difficult to detect, and, by integrating population evolutionary information, infer the functions and evolutionary histories of genes. Together, they provide new perspectives and strategies for dissecting the molecular basis of complex traits in plants. Pan-genomics has become a widely applied tool in recent years. Compared with a single reference genome, a pan-genome enables more comprehensive detection of population-wide single-nucleotide polymorphisms (SNPs) and structural variations (SVs), including copy number variations (CNVs) and presence–absence variations (PAVs). This comprehensive view is critical for understanding the genetic control of phenotypes and for improving complex traits in modern cultivars by exploiting the genetic diversity of wild or distant relatives (Ni et al., 2023). For instance, Benoit et al. selected 22 Solanum species and assembled chromosome-level genomes to address challenges in analyzing orthologous and paralogous genes and their diversification history. They found that over 60% of paralogous gene pairs exhibited either functional redundancy or expression divergence, significantly increasing the difficulty of improving complex traits through natural or engineered mutations. Taking the fruit size gene *CLV3* as an example, its diversification manifests in gene duplication, pseudogenization, and haplotype recombination. These patterns explain key domestication trait differences within and between species and provide a novel framework for systematically uncovering stress-response genes located in the accessory genome (Benoit et al., 2025). Alfalfa, a highly heterozygous autotetraploid outcrossing species, has a highly complex and variable genome, which has severely limited the precise mapping and effective utilization of genes associated with important agronomic traits. Using third-generation sequencing data, haplotype-resolved genome assemblies were generated for 24 alfalfa accessions. Comparative genomic analyses identified approximately 430,000 structural variations, including deletions, insertions, duplications, and inversions, primarily enriched in non-coding regions, leading to the construction of the alfalfa pan-genome. GS analyses of 54 agronomic traits using SVs and SNP markers derived from the pan-genome revealed that SVs provided higher predictive accuracy than SNPs for multiple complex traits. Prediction accuracy for traits related to salt tolerance, growth and development, and forage quality was substantially improved when using SVs. These results underscore the importance of structural variation in dissecting complex traits and molecular breeding, providing new avenues for identifying key genes underlying salt tolerance, growth, and quality in alfalfa (He et al., 2025). The rapid development of pan-genomics and structural variation studies is profoundly reshaping our understanding of the genetic basis of complex traits in plants. Compared with conventional single reference genomes, these approaches not only capture population-wide genetic variation more comprehensively but also reveal previously overlooked deletions and copy number variations. This efficient cycle from variant discovery to functional validation and breeding application offers more feasible and predictable solutions for enhancing crop stress resilience and optimizing trait utilization.

Transcriptomic approaches for stress response analysis

Beyond static genetic variation, plant stress resilience is largely shaped by dynamic molecular responses, with transcriptional regulation playing a central role. RNA-seq, with its broad applicability across species and experimental conditions, has become a powerful tool to investigate crop responses to abiotic stresses such as drought, salinity, heat, and cold. These studies have provided critical insights into underlying regulatory mechanisms and enabled the identification of candidate genes associated with stress tolerance (Lister et al., 2008). While bulk transcriptome analysis provides insights into global gene expression patterns, tissue-level data may obscure cellular heterogeneity and the critical

roles of specific cell types in stress responses. Single-cell transcriptomics enables high-resolution dissection of the molecular mechanisms underlying plant development and stress responses. By profiling gene expression at the cellular level, these methods uncover the contributions of distinct cell types and reveal key determinants of plant growth, stress resilience, and yield potential (Luo et al., 2020; Ritonga and Chen, 2020). Applications in major crops illustrate their potential: In maize, single-cell transcriptomics has been used to uncover genetic variation underlying drought tolerance and disease resilience (Farooqi et al., 2022). While in cotton, combined single-cell transcriptome and assay for transposase-accessible chromatin using sequencing (ATAC-seq) libraries from anthers at the tetrad stage under normal and high-temperature stress revealed key regulatory factors in tapetal cells that mediate heat tolerance (Li et al., 2024). Xue et al. proposed a cross-species single-cell transcriptomics strategy and constructed a plant single-cell atlas covering six species, including lycophytes, ferns, gymnosperms, and angiosperms. They identified a set of evolutionarily highly conserved genes associated with major vascular plant cell types. By integrating single-cell transcriptomes with chromatin accessibility data, they revealed the critical roles of *SECB* and *JULGI-LIKE* genes in sieve element formation and phloem development (Xue et al., 2025). Single-cell transcriptomics can also be used to reveal the transcriptional responses of specific cell types when plants are exposed to various stress conditions. For example, a recent study sampled leaves at different developmental stages and quantified the senescence status of leaf cells at single-cell resolution. This analysis identified cell types that had not been characterized in previous protoplast-based studies and uncovered both conserved and unique features of cell types across different organs. These findings enabled a single-cell level understanding of the molecular mechanisms that control senescence and coordinate nutrient remobilization among organs (Guo et al., 2025). Building on this research framework, further applying single-cell transcriptomic approaches to investigate the dynamic responses of plants to environmental stresses will help to reveal spatiotemporal heterogeneity among cell types and elucidate their roles in signal perception, transduction, and adaptation, thereby deepening the systems-level understanding of plant stress resilience.

Proteomics and metabolomics for decoding stress responses

Metabolic activities in plant cells are self-regulated in response to environmental changes, thereby affecting the synthesis and redistribution of nutrients in crops. Our understanding and ability to manipulate these complex signaling networks are limited by current knowledge of the metabolic pathways involved in these processes (Rossi et al., 2015; Sonnewald and Fernie, 2018). This limitation underscores the need for empirical studies that elucidate how plants modulate their metabolic responses under various stress conditions. For example, Vital et al. revealed through metabolomics analysis that under drought stress, sugarcane responds by regulating the production of secondary metabolites and soluble sugars as well as the scavenging of reactive oxygen species (Vital et al., 2017). Similar applications in maize and sorghum have revealed metabolite adjustments associated with drought stress and photorespiration (Obata et al., 2015; Ogbaga et al., 2016). By linking metabolite profiles with phenotypic traits, researchers can gain a deeper understanding of the molecular basis underlying these phenotypes. Currently, proteomics can qualitatively and quantitatively measure key proteomes in specific cell types or organelles at specific developmental and physiological stages. By revealing protein expression changes and associated signaling pathways in crops under stress, proteomics enables a better understanding of the functions, structures, and developmental dynamics of different proteins across diverse environmental conditions (Kausar et al., 2022; Quan and Liu, 2024).

High-throughput phenomics for large-scale trait characterization

Plant phenotypes are determined by genotype-environment interactions, and environmental factors lead to phenotypic variation. Therefore, collecting large-scale phenotypic data of germplasm resources across diverse environments is a formidable challenge and has become a bottleneck in crop breeding (Dhondt et al., 2013; Tardieu et al., 2017; Yang et al., 2020). At present, the establishment of crop phenomics big-data platforms has emerged as a strategic frontier in agricultural and life sciences (Ninomiya et al., 2019). High-throughput phenotyping technologies enable the efficient acquisition of phenotypic data throughout the entire life cycle of crops. Achieving precise and efficient crop phenotypic characterization is of great significance for elucidating the mechanisms underlying genotype-environment interactions, uncovering intrinsic links between phenotype and genes, and accelerating breeding. A number of modern technologies, such as spectroscopy, imaging techniques, image analysis, and high-performance computing, have been developed for precise phenotypic analysis. Recently, the integration of artificial intelligence algorithms with high-throughput phenotyping data and unmanned aerial vehicle-based phenotypic collection has further transformed this field, making rapid and accurate collection and processing of phenotypic data possible (Ostos-Garrido et al., 2019).

Integrative multi-omics strategies to decipher complex stress responses

Although single-omics approaches have made significant progress in elucidating the genetic and molecular bases of complex traits in plants, environmental stresses in natural conditions are usually not imposed by a single factor but rather by the combined effects of multiple stressors. Under such combined stress conditions, molecular responses are often characterized by extensive interactions and coordinated regulation among gene regulatory networks, signaling pathways, and metabolic processes, which makes it difficult for any single-omics strategy to fully uncover the underlying

mechanisms. Against this backdrop, multi-omics strategies are increasingly becoming essential for understanding plant stress resilience. By integrating data from different layers, including pan-genomics, single-cell transcriptomics, proteomics, and metabolomics, researchers can not only trace the flow of information along the continuum from genetic variation to functional realization but also uncover the interactions across molecular levels under combined stress conditions (Figure 2B). In the process of dissecting rice tillering, a key agronomic trait, integrative multi-omics approaches have demonstrated unique advantages in identifying critical genes and regulatory mechanisms. By jointly analyzing rice population genomic data and microbial metatranscriptomic data, researchers revealed a significant correlation between root-associated microbiota and rice tiller number. Further metabolomic profiling identified functional cyclic dipeptides that can bind to the strigolactone receptor OsD14 and activate downstream signaling, thereby suppressing rice tillering (Shi et al., 2025b). In practice, the effects of combined stresses on plants are not merely the simple addition of individual stresses. In a study of potato responses to combined abiotic stresses at the molecular and physiological levels, integrated analyses of the proteome, transcriptome, and metabolome, together with machine learning, revealed that certain stresses, such as drought and waterlogging, share overlapping signaling pathways. These findings provide important insights into crop adaptation strategies to environmental challenges and offer a valuable basis for breeding climate-resilient varieties (Zagorščak et al., 2025). As multi-omics research continues to advance, phenomics has gradually become a critical link connecting molecular processes with environmental contexts. Genomics, transcriptomics, proteomics, and metabolomics reveal the regulatory mechanisms underlying genetic variation and molecular functions in crops, whereas phenomics enables high-throughput and high-resolution monitoring of plant growth, development, and stress responses throughout the entire life cycle under real environmental conditions. Integrating phenomics with multi-omics datasets and external environmental factors enables researchers to achieve a comprehensive analysis of crop physiological dynamics along the complete continuum from genotype to phenotype. Such multidimensional data integration facilitates the elucidation of the complex interactions among gene regulatory networks, metabolic pathways, and phenotypic traits under genuine combined stress conditions. As research progresses, accumulating evidence has demonstrated that multi-omics strategies possess irreplaceable advantages in elucidating the molecular basis of plant responses under combined stresses (Roychowdhury et al., 2023). On the one hand, the integration of multi-level datasets can overcome the limitations of single-omics approaches in terms of information coverage and explanatory power, thereby establishing a continuous chain from genetic sequences to molecular functions and ultimately to phenotypic manifestations, which more faithfully reflects the dynamic regulatory networks of plants under complex environmental conditions. On the other hand, emerging technologies are continually expanding the scope of multi-omics. For example, transcriptomic and epigenomic analyses at the single-cell level can uncover the heterogeneous responses of distinct cell types to combined stresses, while the incorporation of spatial omics facilitates the delineation of spatiotemporal patterns of signaling and metabolites at the tissue level. The integration of these frontier methods with conventional omics approaches provides an unprecedented resolution for understanding plant stress adaptation (Figure 2B).

DESIGN-DRIVEN STRATEGIES FOR ENGINEERING CLIMATE-RESILIENT CROPS

Conventional crop improvement strategies have predominantly focused on breeding for constitutive tolerance to specific stresses, often relying on the introgression or overexpression of single stress resilience genes. Although effective in some contexts, such approaches impose substantial metabolic and fitness costs under stress-free conditions, ultimately reducing yield potential. With increasing climate variability, it has become evident that crops must evolve beyond static defense mechanisms. A new paradigm is emerging in which crops are designed as dynamic systems capable of sensing, integrating, and responding to environmental cues with high precision. Recent advances in precision genome editing, combined with *de novo* domestication to unlock untapped wild genetic resources, together with the design of synthetic regulatory circuits and optogenetic platforms for spatiotemporal control, provide a powerful and comprehensive toolkit for constructing crops with dynamic environmental responsiveness (Aguirre et al., 2023; Chang et al., 2024; Lou et al., 2025; Figure 3A).

Precision editing technology advances drive the construction of climate-resilient crops

Conventional crop breeding has relied on naturally occurring mutations in regulatory regions, but such mutations are rare and difficult to screen efficiently, limiting the pace of yield-related trait improvement. With the growing global population and shrinking arable land, more efficient and predictable approaches to crop improvement are urgently needed. In this context, researchers have applied CRISPR/Cas9 to target promoter regions—key *cis*-regulatory elements of crop genes. By introducing multiple mutations within promoters, they were able to fine-tune gene expression levels, thereby modulating quantitative traits such as fruit size, branching architecture, and plant morphology (Rodríguez-Leal et al., 2017). This "*cis*-regulatory element editing" strategy generates a continuum of phenotypic variation, expanding the options available for breeding. The findings advance the development of precision breeding technologies and represent a significant contribution to sustainable agriculture and climate resilience.

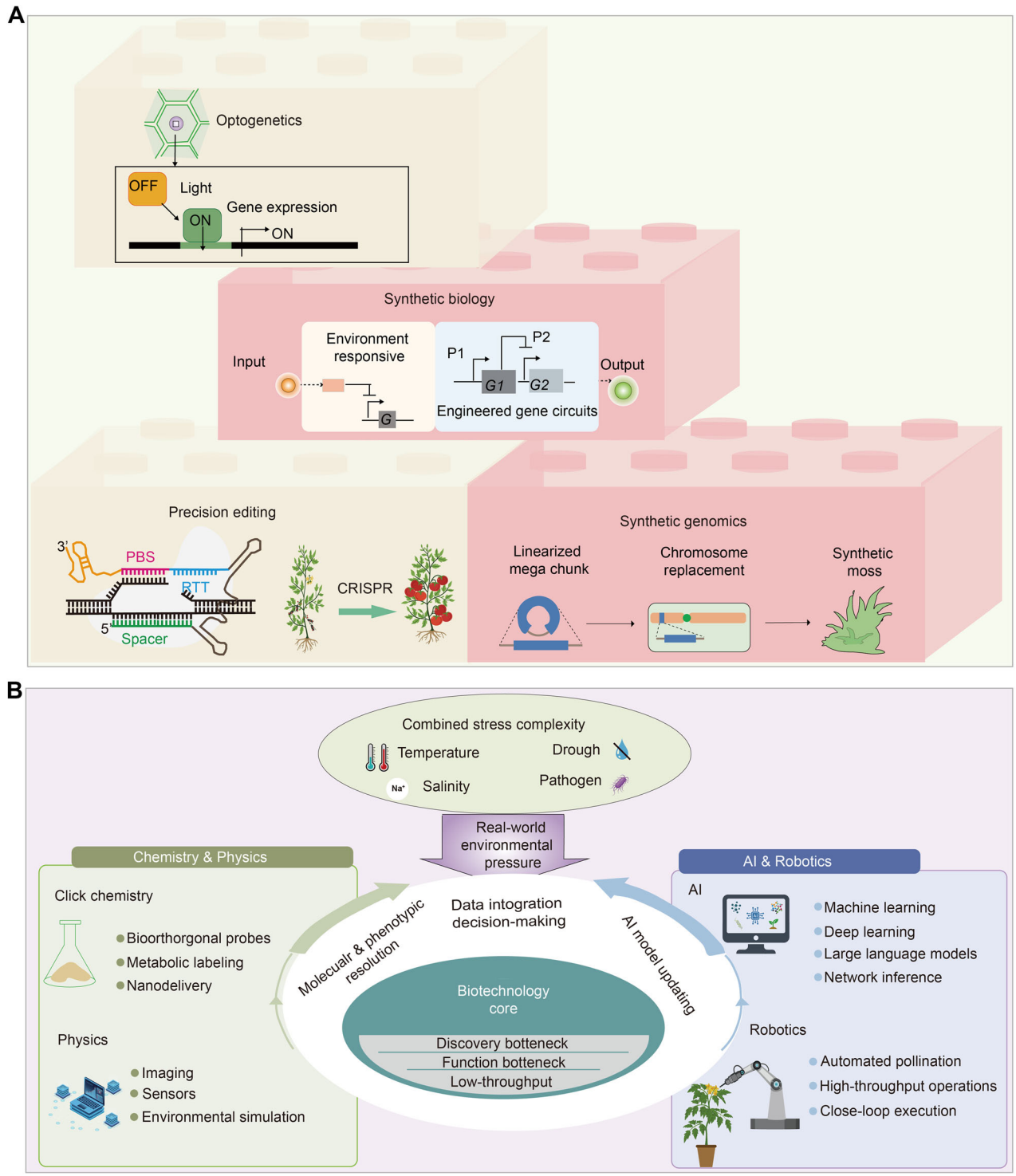

Figure 3. Design-driven strategies and interdisciplinary technologies for climate-resilient crops
(A) Rational design and precision engineering for climate-resilient crops. Precision editing, synthetic genomics, synthetic biology, and optogenetics—each module is depicted in a "Lego-style" visual metaphor to emphasize flexibility and combinatorial assembly. **(B)** Interdisciplinary tools and platforms empowering crop biotechnology.

Advances in genomics have revealed that SNPs and small-scale sequence variations strongly shape agronomic traits and stress adaptability. Base editing (BE) extends genome engineering beyond simple knockouts by introducing targeted nucleotide substitutions without double-strand breaks (Rees and Liu, 2018; Yang et al., 2019; Zhu et al., 2020; Newby and Liu, 2021). This allows precise modification of amino acids, *cis*-regulatory motifs, or stress-related SNPs

in plants (Shimatani et al., 2017; Zong et al., 2017, 2018). Currently, applications of base editing in crop improvement have been most extensively demonstrated in rice, but are increasingly being extended to other major crops such as wheat, maize, rapeseed, tomato, potato, and watermelon (Bharat et al., 2020). Most efforts have focused on the targeted modification of well-characterized functional genes to enhance yield, improve stress resilience, and optimize quality traits. For instance, editing of the *NRT1.1B* gene, which regulates nitrogen transport, has been shown to increase nitrogen use efficiency and promote yield gains. Modification of *SLR1* reduces plant height and thereby enhances lodging resilience in rice (Lu and Zhu 2017; Zong et al., 2017). Moreover, base editing of the *ALS* gene, which is highly conserved across plant species, has conferred herbicide resilience in multiple crops, providing a broadly applicable strategy for trait improvement (Zhang et al., 2019; Wu et al., 2020).

While BEs excel at transitions, they cannot efficiently introduce transversions, insertions, or deletions. Prime editing (PE) further expands the scope to transversions, small insertions, and deletions, making it powerful for fine-tuning promoter architectures and regulatory modules (Anzalone et al., 2019). The fundamental principle involves fusing nCas9 with a reverse transcriptase (RT) and employing a structurally engineered prime editing guide RNA (pegRNA) to simultaneously direct target site recognition and provide the editing template. Recent studies have further demonstrated the substantial potential of PE technology in crop genetic improvement (Figure 3A). Zou et al. developed a robust multiplex gene editing tool named the Cas9-PE system, which enables simultaneous precise editing and site-specific random mutagenesis in rice. By employing targeted modification of the endogenous *ALS* gene as a selectable marker to confer herbicide resilience, the system achieved multigene editing in the T0 generation without residual exogenous transgenic elements. These results provide a powerful methodological framework to support molecular design breeding (Zou et al., 2025). This system enables the simultaneous achievement of precise editing and site-specific random mutagenesis at the T0 generation, while generating edited plants free of exogenous transgenic components, thereby conferring high practicality and biosafety. With further optimization and refinement, the Cas9-PE platform is expected to be extended to a broader range of crops, particularly perennial, vegetatively propagated, and apomictic species, which will substantially accelerate the progress of crop improvement. A key challenge in developing climate-resilient crops is to decouple development from stress-induced hypersensitive responses, thereby enabling plants to autonomously optimize assimilate distribution in response to environmental fluctuations, achieving high yield under favorable conditions and yield stability under stress. Addressing this challenge, Lou et al. developed a "Climate-Responsive Carbon Allocation Optimization System" (CROCS) in tomato and rice, employing PE to precisely insert heat-shock element (HSE) into the promoter regions of cell wall-invertase (CWIN). The introduced HSE did not alter the spatial expression pattern of *LIN5* but conferred heat-inducible upregulation. Carbon isotope tracing experiments demonstrated that HSE knock-in enhanced sucrose transport to fruits, markedly alleviating heat-induced "sugar starvation", thereby endowing tomato with an environmentally responsive mechanism to dynamically expand sink capacity and maintain assimilate flow (Lou et al., 2025). Over the past decades, basic plant science has identified numerous *cis*-regulatory elements responsive to biotic and abiotic stresses, nutrient uptake and utilization, and symbiotic interactions. These elements respond to diverse stimuli, including heat, cold, drought, salinity, light, pathogen infection, and nutrient deficiency (Liu et al., 2014). By providing a robust framework for the precise knock-in of such environmentally responsive molecular switches, CROCS paves the way for the development of climate-resilient crops while also offering a powerful tool and methodological platform for dissecting the mechanisms of plant developmental adaptation to environmental change. To achieve precise improvement of crop traits, it is essential to first pinpoint the key determinants underlying trait formation. Xu et al. systematically traced the evolutionary trajectory of coenzyme Q in land plants and analyzed natural variation in its core biosynthetic enzymes, thereby elucidating the molecular mechanism controlling coenzyme Q side-chain length. Using prime editing, the authors introduced five amino acid substitutions in the rice Coq1 enzyme, successfully generating new rice germplasm capable of synthesizing coenzyme Q10. This work integrates evolutionary genomics, molecular dissection, and precision editing, establishing a paradigm for rational trait design. Beyond creating CoQ10 rice, it demonstrates how natural evolutionary trajectories can inform the targeted reconfiguration of plant metabolic pathways, offering a blueprint for designing climate-resilient and nutritionally enhanced crops (Xu et al., 2025). Although advanced systems such as PE have greatly expanded the capacity for precise genome editing, technical bottlenecks remain in achieving the stable, site-specific, and seamless insertion of large DNA fragments. To overcome this limitation, researchers have turned their attention to a novel tool that has co-evolved with the CRISPR system—the CRISPR-associated transposases (CASTs) system (Ravindran, 2012; Hickman and Dyda, 2016). Previous studies have fused the Pong transposase derived from rice with Cas9 or Cas12a systems to establish a programmable CASTs platform, enabling the precise insertion of enhancer elements, open reading frames, and expression cassettes in *Arabidopsis thaliana* and soybean (Liu et al., 2024b). Compared with the PE system, CASTs not only achieve higher insertion efficiency but also provide greater flexibility in insertion length and target site selection, making them particularly suitable for inserting functional sequences such as stress-responsive elements and artificial regulatory modules into promoter regions, thereby enabling the development of smart crops with environmental sensing and adaptive regulation capabilities.

De novo domestication for engineering climate-resilient crops

Precision genome editing technologies have provided powerful tools for targeted trait modification, but historical domestication and natural selection still constrain the available genetic potential in many existing crops. To break this bottleneck, *de novo* domestication has emerged as a novel design-driven strategy that systematically reshapes crop genomes to unlock and utilize wild genetic resources, offering a new avenue for the rapid development of highly adaptive crops (Kumar et al., 2021). Unlike conventional domestication, which often results in the loss of valuable stress tolerance traits from wild species, this approach leverages genome editing to introduce key domestication and agronomic traits directly into wild or semi-wild species. By precisely modifying loci associated with plant architecture, flowering time, yield, and nutritional quality, breeders can create cultivars that retain the inherent resilience of wild germplasm while acquiring the agronomic characteristics necessary for large-scale cultivation. This strategy not only accelerates the lengthy process of conventional domestication but also improves the predictability of trait integration and cultivar improvement (Li et al., 2018; Zsögön et al., 2017, 2018). Proof-of-concept studies have demonstrated the feasibility of this approach across multiple crops. For example, in *Solanum pimpinellifolium*, a wild tomato species that is naturally tolerant to salinity and bacterial spot disease, multiplex CRISPR Cas9 was used to target genes controlling flowering photoperiod sensitivity, plant architecture, fruit synchronous ripening, fruit size, and ascorbate biosynthesis. The edited lines exhibited compact double determinate architecture, improved fruit set and synchronized ripening, and higher harvest index, thereby accelerating the domestication of the wild species (Li et al., 2018). Similarly, in wild allotetraploid rice, editing genes that regulate seed shattering, plant height, grain length, and flowering time have produced novel rice lines combining high yield with enhanced environmental adaptability (Yu et al., 2021). Moreover, *de novo* domestication can be integrated with conventional hybrid breeding techniques to leverage their complementary advantages, establishing a combined rapid breeding strategy. For instance, Xie et al. demonstrated a dual strategy in tomato: genome editing was used to generate male sterile lines in cultivated varieties to reduce hybrid seed production costs, while *de novo* domestication was simultaneously applied to stress-tolerant wild accessions. This dual approach not only streamlined hybrid breeding but also facilitated the efficient use of wild and cultivated germplasm, accelerating the development of stress-resilient cultivars (Xie et al., 2022).

Rational design of genetic networks and synthetic modules for crop improvement

Accelerating crop improvement requires not only harnessing traits shaped by natural evolution but also implementing transformative engineering based on mechanistic understanding to establish resilient production systems that secure future harvests. Since the advent of plant biotechnology, the prospect of conferring enhanced functions on plants through engineering approaches has been particularly compelling, and this vision has become increasingly critical under the pressures of climate change and global population growth. Many complex traits are governed by genetic circuits rather than single genes. Synthetic biology, which integrates principles of engineering with biology, physics, chemistry, and computational science, provides a framework for purposefully modifying existing biological systems or creating entirely new input–output traits in crops (Bartley et al., 2017). Researchers have been developing strategies to reprogram plant biological processes to enable more efficient growth under diverse conditions. For example, a suite of synthetic transcriptional regulators and synthetic promoters has been engineered to construct genetic logic circuits. Among them, BUFFER circuits demonstrated the potential of synthetic regulatory networks by quantitatively controlling lateral root density in Arabidopsis, thereby showcasing their capacity to modulate cross-tissue gene expression and reprogram plant development (Brophy et al., 2022). Shi et al. designed multiple BUFFER circuits incorporating synthetic transcriptional regulators. Their feasibility was first validated in *Nicotiana benthamiana* leaves and subsequently applied in soybean, where seed-specific expression increased melatonin content by 31-fold relative to the wild-type Williams 82, accompanied by higher protein content, reduced oil content, and enhanced post-harvest processing quality, without compromising yield. Importantly, this modification also conferred greater salt tolerance to soybean seeds. In cotton, the circuits elevated endogenous melatonin levels, improving resilience to verticillium wilt (Shi et al., 2025c). These works highlight the promise of synthetic genetic circuits for engineering staple crops with targeted metabolite accumulation and for developing novel crop varieties that couple nutritional enhancement with environmental adaptability.

Synthetic genomics is an emerging branch of synthetic biology that seeks to chemically synthesize entire chromosomes and genomes, and to replace their natural counterparts within cells (Figure 3A). The ultimate goal is to create novel life forms for innovative applications while also deepening our understanding of fundamental biological processes (Wang et al., 2018b; Fu and Shen, 2024). Over the past decades, synthetic genomics has achieved remarkable milestones in the *Saccharomyces cerevisiae* 2.0 (Sc2.0) project, which generated the first eukaryotic organism carrying fully *de novo*-designed synthetic chromosomes (Pretorius and Boeke, 2018). In contrast, plant synthetic genomics faces greater challenges due to the complexity of plant genomes. Recently, researchers adopted the model plant *Physcomitrium patens* as a platform to redesign its chromosome sequences, achieving extensive genome minimization by removing 55.8% of endogenous sequences and introducing artificial tags. The redesigned sequences were synthesized and assembled, with approximately one-third of a chromosomal arm successfully replaced *in vivo*. The resulting synthetic lines displayed normal growth and reestablished a typical epigenetic landscape across the synthetic regions, thereby laying the groundwork for the large-scale *SynMoss* synthetic genome project and paving the way for gene synthesis in multicellular organisms

(Chen et al., 2024). Yu et al. outlined the design principles of the synthetic *P. patens* genome and developed GenoDesigner, an online tool for genome-wide sequence editing and redesign. Using this platform, they completed the first version of the SynMoss genome, providing not only a foundation for synthetic moss genomics but also a broadly applicable resource for the design of other synthetic genomes (Yu et al., 2024). Importantly, future synthetic chromosomes will incorporate essential genetic elements such as artificial centromeres and telomeres and are envisioned as independently heritable units in plant cells. This advancement opens up powerful new possibilities for endowing crops with complex traits such as enhanced climate adaptability.

Optogenetics, a technology that employs light-sensitive proteins to precisely regulate molecular and cellular processes, is gradually expanding into plant science and smart breeding. Its high spatiotemporal resolution and reversibility enable researchers to finely control gene expression and signaling pathways at the cellular or tissue level, thereby modulating crop traits. For example, expression of the BLINK1 tool in Arabidopsis guard cells accelerated stomatal opening and closing under fluctuating light conditions, resulting in nearly a twofold increase in biomass without compromising water-use efficiency (Papanatsiou et al., 2019). The application of *GtACR1* in tobacco guard cells enabled light-controlled stomatal closure, offering a promising strategy for breeding drought-tolerant and water-saving crops, as activation of anion channels under drought or high-light conditions can force stomatal closure to reduce water loss (Huang et al., 2021). In addition, the development of optogenetic gene expression switches such as the PULSE system allows effective regulation of gene expression under standard white-light growth conditions without chemical inducers, greatly enhancing practicality and reliability (Ochoa-Fernandez et al., 2020). Coupling optogenetics with CRISPR/Cas9, multi-omics, and high-throughput phenotyping platforms holds promise for precise improvement of traits, including drought tolerance, thermal adaptation, photosynthetic efficiency, architecture, and flowering time. Future progress will rely on engineering proteins with enhanced expression or optimized localization, refining cofactor biosynthesis, and exploiting spectral ranges minimally perceived by endogenous photoreceptors to reduce background interference. Together, these advances position optogenetics as a versatile strategy for next-generation crop breeding.

INTERDISCIPLINARY APPROACHES EMPOWERING BIOTECHNOLOGY FOR CLIMATE-RESILIENT CROPS BREEDING

In the process of breeding climate-resilient crops, biotechnology undoubtedly serves as the core driving force, directly determining the discovery of new genes, functional characterization, and the feasibility of targeted improvement (Rivero et al., 2022). However, relying solely on traditional biological research methods is often constrained by experimental scale, operational efficiency, and technological boundaries, limiting their potential to fully address complex environments and multiple stress conditions (Straathof et al., 2019). In recent years, with the acceleration of interdisciplinary integration, cutting-edge technologies from chemistry, physics, artificial intelligence, and robotics have been increasingly applied to crop science research, providing unprecedented empowerment to biotechnology and significantly enhancing its efficiency, precision, and breadth of application (Holzinger et al., 2023; Figure 3B). These emerging technologies complement biological approaches, acting as amplifiers and accelerators, enabling biotechnology to operate more rapidly and accurately, thereby substantially advancing the development of climate-adaptive varieties.

Chemical and physical innovations enhancing molecular-level breeding

In the process of empowering biotechnology to drive climate-resilient crop breeding, chemistry and physics, as two fundamental disciplines, provide complementary tools and methods at the molecular level and the environmental-phenotypic level, respectively. Together, they expand the application boundaries of biotechnology and significantly enhance its efficiency and precision. The core value of chemistry lies not only in providing experimental tools but also in reshaping our understanding of crop-environment interactions at the molecular scale. Advances in synthetic chemistry and chemical biology have continuously expanded novel molecular probes and modification strategies, enabling researchers to track the dynamic changes of signaling molecules, hormones, and metabolites under complex stress conditions, thereby elucidating the regulatory networks underlying key phenotypes of crop responses to diverse stresses (De Rybel et al., 2009; Loewith et al., 2021). The integration of analytical chemistry with metabolic labeling techniques further facilitates the elucidation of metabolic reprogramming in plants under stress and the identification of novel targets for molecular breeding (Singha et al., 2021). Moreover, progress in materials chemistry and nanotechnology has created opportunities for developing delivery systems for signaling molecules. These chemical innovations not only extend the scope of biotechnology but also provide more efficient and precise technological pathways for environmentally adaptive breeding (Yao et al., 2014). Notably among various chemical approaches, click chemistry stands out as a representative innovation. Characterized by high efficiency, specificity, and mild reaction conditions, it has been described as a “molecular Lego” and was awarded the Nobel Prize in Chemistry in 2022. Click chemistry enables the rapid and selective conjugation of molecular units within biological systems without perturbing native biochemical processes. Notably, Bertozzi's development of bioorthogonal chemistry allows labeling and tracking of molecules in living systems, providing a novel perspective for plant science and empowering biotechnology to dissect molecular responses of

crops under stress at greater depth (Bertozzi, 2011). For instance, incorporating click reactions into miRNA detection can overcome the sensitivity limitations of conventional approaches, facilitating the identification of key regulators involved in stress responses (Fan et al., 2018). In proteomic studies, click chemistry combined with activity-based probes (ABPs) enables efficient labeling of target proteins without affecting enzymatic activity, followed by analysis of complex protein networks through mass spectrometry or imaging. This is essential for elucidating signal transduction pathways and stress regulatory mechanisms under drought, salinity, or heat stress (Martell and Weerapana, 2014). Furthermore, when integrated with metabolic glycan labeling (MGL), fluorescence imaging, or affinity probes, click chemistry enables *in vivo* labeling and visualization of glycoproteins, polysaccharides, and other biomacromolecules, offering dynamic monitoring capabilities while minimally interfering with normal plant physiology. In rice, the combination of click chemistry and affinity probes enabled the enrichment of N-azidoacetylgalactosamine (GalNAz)-labeled glycoproteins, leading to the identification of 403 N-glycosylation sites and 673 N-glycosylated proteins through mass spectrometry. These proteins were found to be extensively involved in endoplasmic reticulum-associated degradation (ERAD) pathways and other essential biological processes (Lei et al., 2025). Thus, by enabling real-time monitoring of glycoprotein modifications, cell wall polysaccharide deposition, and signaling molecule distribution, click chemistry provides a powerful means to unravel the molecular regulatory strategies of crops under stress and offers crucial molecular insights into stress resilience. Meanwhile, physical technologies empower biotechnology from a macroscopic perspective, particularly by providing indispensable support in environmental simulation and high-throughput phenotyping, thereby enabling more efficient and precise gene discovery, functional characterization, and targeted improvement under complex environmental conditions. In particular, physics occupies an irreplaceable position in high-throughput phenotyping. Techniques such as optical imaging, near-infrared imaging, fluorescence imaging, thermal imaging, and magnetic resonance imaging enable noninvasive monitoring of crop growth, leaf water status, root architecture, and disease progression, providing reliable means for the large-scale acquisition and analysis of phenotypic data (Gurfinkel et al., 2003; Li et al., 2014). When integrated with genomic datasets, these fine-scale phenotypic insights can significantly enhance the resolution of complex trait analysis and improve the accuracy of stress-resilience trait selection.

AI and robotics platforms for precision accelerated crop breeding

In recent years, multiple artificial intelligence (AI)-enabled breeding tools have been successively developed. For example, in rice, by constructing the world's largest curated research database and utilizing the Alibaba Qwen2.5-7B model as the foundation, researchers applied training and fine-tuning procedures to develop the Fengdeng Rice Seed Industry large language model (SeedLLM). This platform focuses on key topics such as gene function, hybrid breeding, and molecular design, thereby providing a novel AI-based tool (Yang et al., 2025). The intelligent breeding platform AutoGP enables the selection of high-quality single-nucleotide polymorphisms (SNPs) and can be integrated with GS modules. It encompasses five core functional modules: model training, phenotype prediction, integrated training and prediction, optimal parental selection, and integrated training and selection. By choosing different machine learning or deep learning models, AutoGP determines the most suitable GS framework for unified phenotype prediction across diverse environments, thus markedly improving model adaptability and applicability (Wu et al., 2025). In protein design, AI approaches have demonstrated substantial advantages in identifying potentially high-fitness mutations within the vast protein sequence space. Reverse folding models, such as ESM-IF1 and ProteinMPNN, learn the complex distribution patterns of natural protein sequences and structures, and can directly generate high-confidence amino acid sequences compatible with specific backbone architectures. Furthermore, the AI-informed constraints for protein engineering (AiCE) computational framework enhances efficiency and scalability, enabling rapid optimization of diverse genome editing tools (Fei et al., 2025). In chromosome engineering, AI contributes to the efficient design and optimization of editing strategies. The AI-assisted recombinase engineering platform (AiCErec) achieves significantly improved recombination efficiency by optimizing Cre recombinase variants, while programmable chromosome engineering (PCE) and the scar-free chromosome editing strategy (RePCE) integrate prime editing, recombination site design, and genome rearrangement to enable insertions, deletions, substitutions, inversions, and translocations ranging from kilobase to megabase scales (Sun et al., 2025). Xie et al. first applied genome editing to redesign floral morphology in crops, thereby rapidly and precisely generating male sterile lines. They subsequently developed an intelligent pollination robot, GEAIR, which employs the deep learning network YOLACT_Orient to achieve high-precision recognition of flowers and stigmas, enabling complete automation of the hybrid breeding process. This system operates continuously under all conditions, drastically reduces labor costs, and markedly improves pollination efficiency. The intelligent breeding framework has been successfully applied not only in tomato but also in other crops, establishing a model that is grounded in biotechnology, supported by AI for data modeling and intelligent analysis, and enabled by robotics to achieve practical operations and automation. This proprietary, closed-loop intelligent robotic breeding system realizes fully integrated management from floral design to automated pollination. Such interdisciplinary integration not only promotes the widespread application of heterosis but also provides scientific and technological support for the intelligent development of environmentally adaptive breeding in the future (Xie et al., 2025).

Overall, the continuous introduction of frontier technologies from disciplines such as chemistry, physics, artificial intelligence, and robotics has further amplified and expanded the role of biotechnology in breeding environmentally adaptive crops (Figure 3B). On the one hand, with ongoing advances in synthetic chemistry, nanomaterials, and bioorthogonal chemistry, the operational scope of biotechnology at the molecular level will become increasingly extensive. On the other hand, with the continuous development of imaging physics and sensing technologies, crop phenotyping will become more multidimensional and dynamic, providing higher resolution support for the improvement of complex traits. At the same time, the iterative progress of artificial intelligence and robotic systems is expected to promote crop breeding toward full-process intelligence and automation, thereby forming a closed-loop model that connects design with implementation. Collectively, these interdisciplinary technologies provide systematic empowerment to biotechnology, enabling a qualitative leap in the efficiency, precision, and scale of breeding environmentally adaptive crops.

TOWARD AN INTELLIGENT CLOSED-LOOP BREEDING SYSTEM

Taken together, the advances described above point toward the emergence of an intelligent closed-loop breeding framework that integrates data acquisition, knowledge discovery, rational design, and rapid validation. In this framework, large-scale datasets are generated through multi-omics profiling, high-throughput phenotyping, and environmental monitoring. Advances in chemistry enable the detection of stress-responsive metabolites and signaling molecules, while physics-based sensing technologies and imaging platforms capture dynamic phenotypic responses across diverse environments. These multidimensional datasets can then be analyzed using genome-wide association studies, multi-omics integration, and machine learning approaches to enable precision identification of key genes, regulatory elements, and favorable alleles underlying target traits. The resulting knowledge provides the basis for design-driven breeding, in which optimal genetic architectures are rationally assembled using genome editing, synthetic biology, and computational prediction, including AI-assisted parent selection. Subsequently, accelerated breeding strategies, such as speed breeding, doubled haploids, and genomic selection, allow rapid generation and evaluation of breeding materials. At the same time, robotic and automated platforms can facilitate large-scale phenotyping and hybridization with reduced labor input. Importantly, phenotypic performance and environmental response data generated during these processes can be continuously fed back into predictive models, enabling iterative optimization of breeding decisions and gradually forming a dynamic closed-loop system for crop improvement.

Although a fully integrated closed-loop breeding system remains largely conceptual at present, several studies have demonstrated partial implementation of this framework. For example, Lou et al. developed the CROCS system by introducing heat-responsive regulatory elements into the promoter of the *CWIN*, enabling environment-responsive carbon allocation under heat stress (Lou et al., 2025). Xie et al. combined genome editing with the intelligent pollination robot GEAIR, enabling automated flower recognition and hybridization and demonstrating the integration of molecular design, AI, and robotics in practical breeding pipelines (Xie et al., 2025). These examples illustrate how current technologies can be combined to implement key elements of the closed-loop concept, providing a foundation for future development of fully integrated intelligent breeding systems.

CHALLENGES AND FUTURE DIRECTIONS

Despite these promising developments, substantial challenges remain before such integrated systems can be widely implemented in crop breeding. First, the performance of many biotechnology-based breeding strategies remains strongly influenced by genome–phenome–environment ($G \times P \times E$) interactions. Traits identified under controlled experimental conditions may exhibit variable performance across diverse field environments, particularly under compound and sequential stress scenarios. Improving environmental modeling, multi-location trials, and predictive frameworks that integrate genome–phenome-environment interactions will therefore be essential to ensure the stability and reliability of breeding outcomes. Second, design-driven breeding approaches, including genome editing, synthetic biology, and optogenetics, face technical limitations. Efficient multiplex editing of polygenic traits remains challenging due to editing efficiency constraints, potential off-target effects, and complex epistatic interactions among modified loci. In addition, the long-term field stability and ecological safety of synthetic regulatory elements or engineered metabolic pathways require careful evaluation before large-scale agricultural deployment. Third, the integration of interdisciplinary technologies such as AI, robotics, and advanced phenotyping platforms into breeding pipelines remains incomplete. Limited data standardization, interoperability among digital platforms, and intellectual property constraints often hinder efficient data sharing and collaborative innovation across institutions (Table 2).

Moreover, the accessibility of advanced breeding technologies represents an important but often overlooked challenge. Many emerging tools—including high-throughput phenotyping systems, AI infrastructure, and robotic platforms—require substantial technical expertise and financial investment. This may widen the technological gap between well-resourced institutions and smaller breeding programs, particularly in developing regions that are most vulnerable to climate change. Future progress will therefore depend not only on technological breakthroughs but also on the development of inclusive innovation strategies, including

Table 2. Key technological limitations and corresponding future research directions across major breeding modules.

Research focus	Key challenges	Future research prioritie
G × P × E integration	Unstable trait expression under variable field conditions	Predictive models and experimental networks integrating multi-stress field data
Design-driven breeding	Limited editing precision, epistasis complexity	Multiplex genome editing, functional validation of synthetic pathways
Interdisciplinary integration	Fragmented data pipelines	Unified digital breeding platforms linking AI, phenotyping, and robotics
Equity and accessibility	Technological divide among institutions	Open-source tools, shared infrastructure, and collaborative efforts
Genetic diversity use	Underutilized germplasm	Re-domestication, pan-genomic analysis, and synthetic germplasm design

low-cost phenotyping tools, open-source analytical platforms, shared data infrastructures, and international collaborative breeding networks (Table 2). Addressing these challenges will be critical for translating the promise of biotechnology-driven breeding into sustainable agricultural solutions under rapidly changing climate conditions.

CONCLUSIONS

The accelerating challenges of climate change and global food demand is fundamentally reshaping crop stress landscapes. Critically, the most pressing challenge for agriculture in the coming decade will not be isolated stresses but compound and sequential stress combinations—such as drought accompanied by heat waves, salinity followed by flooding, or abiotic stress preconditioning crops for disease outbreaks—that generate nonlinear, amplified yield losses and undermine the predictability of breeding outcomes (Mittler, 2006; Zandalinas et al., 2021). In this review, we highlight four converging technological pathways—accelerated breeding, precision identification of stress-resilience modules, design-driven breeding strategies, and interdisciplinary technological integration—that collectively enable a new paradigm for climate-resilient crop improvement. Together, these advances point toward the emergence of intelligent breeding frameworks capable of integrating genome–phenome-environment information and enabling data-driven decision-making. Equally important is the systematic conservation and innovative use of genetic diversity—ranging from landraces to wild relatives—through strategies such as re-domestication, synthetic biology, and advanced material-enabled transformations.

At the same time, realizing this vision will require overcoming key biological, technological, and institutional challenges. Equally important is ensuring equitable access to emerging breeding technologies. Developing cost-effective tools, open data infrastructures, and international collaborative platforms will be essential for extending the benefits of climate-resilient breeding to resource-limited regions and smaller breeding programs. In this context, climate-resilient breeding should be viewed as a complex engineering endeavor that transcends disciplinary boundaries. By integrating biotechnology with data science, systems biology, and global collaboration, crop breeding can move beyond reactive responses toward proactive adaptation to compound stress landscapes. Embedding multifactorial stress resilience into breeding design will provide a critical pathway toward sustainable yield improvement and global food security under accelerating climate uncertainty.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

C.X. conceived the article and revised the manuscript. Z.W. and D.Y. drafted the manuscript. All authors have read and approved the contents of this paper.

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