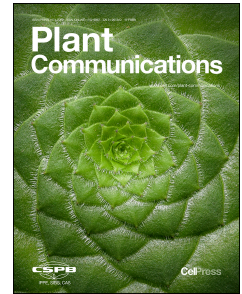


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Cropformer: An Interpretable Deep Learning Framework for Crop Genome Prediction

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1 **Cropformer: An Interpretable Deep Learning Framework for Crop Genome**
2 **Prediction**

3
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1 **Summary**

2 Machine learning and deep learning have become transformative tools in genomic
3 selection (GS) to improve prediction accuracy and accelerate crop breeding.
4 Cropformer, a novel deep learning framework combining convolutional neural
5 networks and self-attention mechanisms, demonstrates superior performance in
6 predicting phenotypic traits across five major crops. By improving prediction
7 robustness and interpretability, Cropformer assists gene mining and supports genomic-
8 assisted breeding strategies.

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1 Abstract

2 Machine learning and deep learning have been employed in genomic selection (GS) to
3 expedite the identification of superior genotypes and accelerate breeding cycles.
4 However, a significant challenge for current data-driven deep learning models in GS is
5 their low robustness and interpretability. To address this challenge, we developed
6 Cropformer, a deep learning framework for predicting crop phenotypes and exploring
7 downstream tasks. The framework consists of a combination of convolutional neural
8 networks and multiple self-attention mechanisms to improve accuracy. Here,
9 Cropformers ability to predict complex phenotypic traits was extensively evaluated on
10 more than 20 traits across five major crops: maize, rice, wheat, foxtail millet, and
11 tomato. Evaluation results show that Cropformer outperforms other GS methods in
12 precision and robustness. Compared to the runner-up model, Cropformer's prediction
13 accuracy improved by up to 7.5%. Additionally, Cropformer enhances the ability to
14 analyze and assist the mining of genes associated with traits. With Cropformer, we
15 identify dozens of single nucleotide polymorphisms (SNPs) with potential effects on
16 maize phenotypic traits and reveal key genetic variations t underlying these differences.
17 Cropformer makes considerable advances in predictive performance and assisted gene
18 identification, representing a powerful general approach to facilitating the genomic
19 design of crop breeding. Cropformer is freely accessible at <https://cgris.net/cropformer>.

20 **Keywords:** Deep learning; Genomic selection; Multiple self-attention mechanisms;
21 Phenotypic prediction;

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2 **Introduction**

3 By 2050, approximately 9 billion people will live on earth, and utilizing limited
4 resources is a serious challenge for ensuring the demand for global food production can
5 be met(Wallace et al., 2018). Furthermore, changing lifestyles, altered population
6 demographics, deterioration of natural resources, climate change, and diminished water
7 supplies are equally challenging problems for crop breeders aiming to achieve precision
8 plant breeding to improve crop performance(Hickey et al., 2017). With the
9 advancement of next-generation sequencing technologies, knowledge acquired from
10 basic plant biology research has dramatically enhanced our understanding of the
11 structure and function of plant genomes and has accelerated crop improvement in recent
12 decades(Varshney et al., 2005). However, the time-consuming nature and even inability
13 to capture "minor" genetic effects in marker-QTL associations remain the major
14 barriers to the selection of suitable breeding materials(Desta and Ortiz, 2014; Xu et al.,
15 2012).

16 The introduction of genomic selection (GS) has paved the way for overcoming these
17 limitations through the use of whole-genome prediction models(Ma et al., 2018). GS
18 was initially proposed by Meuwissen et al. to improve breeding efficiency by reducing
19 phenotyping costs and shortening the cycle time for early-generation
20 selection(Meuwissen et al., 2001). GS utilizes machine learning to determine the
21 correlation between phenotypic data and high-density molecular markers, such as
22 single nucleotide polymorphisms (SNPs), in the training population(Tong et al., 2020).
23 The model was subsequently used to predict genomic estimated breeding values
24 (GEBV) for genotypes in the test population(Habyarimana et al., 2020; Werner et al.,
25 2020). Most importantly, GS allows for the consideration of minor-effect QTLs that
26 cannot be detected by traditional association methods, thus improving the ability to
27 predict these QTLs and drastically reducing the duration of the breeding process(Tong
28 and Nikoloski, 2021). Such advances in genotyping techniques are allowing samples to

1 be genotyped at a lower cost, and GS in particular is actively being incorporated into
2 plant breeding(Krishnappa et al., 2021).

3 Over the last few decades, a series of models using statistics and machine learning
4 have been well advanced in genome prediction based on genome
5 sequences(Covarrubias-Pazaran, 2016; Endelman, 2011a; Miszta, 2008). For instance,
6 ridge regression BLUP (rrBLUP), using linear mixed-effects models to infer genomic
7 kinship and marker effects in breeding material for phenotypic prediction(Endelman,
8 2011b). Expanding on Light Gradient Boosting Machines (LightGBM), Yan et al.
9 developed CropGBM to achieve genotype-to-phenotype prediction. With a large
10 dataset of inbred and hybrid maize lines, CropGBM exhibited superior performance in
11 terms of prediction precision, model stability, and computing efficiency(Yan et al.,
12 2021). In addition to the above methods, there are many other deep learning-based
13 genome prediction methods such as DEM(Ren et al., 2024), DNNGP(Wang et al.,
14 2023b), DeepGS(Ma *et al.*, 2018) and SoyDNGP(Gao et al., 2023). Although deep
15 learning has been successfully applied to whole-genome prediction, current methods
16 still follow a "black-box" model and lack interpretability. This limitation restricts our
17 ability to understand the relationship between features and prediction outcomes.
18 Additionally, the predictive accuracy and training efficiency can be further improved.

19 Here, we present Cropformer, a GS framework that combines convolutional neural
20 network and self-attention mechanism. Evaluation showed that Cropformer
21 outperformed all other methods in the prediction of both discrete and quantitative traits.
22 Comparing with previous deep learning-based GS algorithms, Cropformer can assess
23 the correlation between variations and crop traits with high resolution, facilitating the
24 understanding of the "black-box" mechanisms of deep learning models. In summary,
25 we present a deep learning-based method in conjunction with genomic big data for
26 genomic prediction in crops with improved accuracy, supporting the interpretation of
27 key variations associated with phenotypes that have not been previously reported and
28 suggesting a promising future for understanding how the genome produces phenotypes.

1

2 **Results**

3 **Design of Cropformer**

4 To predict complex phenotypic traits in crops, we developed and trained a deep neural
5 network model, namely Cropformer (Figures 1, and S1). Cropformer takes the
6 sequences of SNPs from genomic variation data and phenotypic values as input to train
7 and make predictions (Figure 1A). The core components of Cropformer consists a
8 convolutional neural network (CNN) layer and a multiheaded self-attention mechanism
9 (Figure 1B). The convolution layer of CNN can automatically extract features from the
10 raw input data and map them into information representations during the training
11 process without human intervention(Krizhevsky et al., 2017). It transforms the input
12 genomic data into informative representations, optimizing the model's learning during
13 training. The output features of the CNN are fed into the attention module to obtain a
14 decision vector for prediction. To demonstrate the effectiveness of integrating CNN and
15 the multiheaded self-attention mechanism in improving prediction, an ablation study
16 was performed, which resulted in the pearson correlation coefficient (PCC) of
17 Cropformer on the Maize data being 92.21% for days to tasselling (DTT), 91.82% for
18 plant height (PH), and 76.31% for ear weight (EW), which were 10.6%, 3.9%, and 6.9%
19 higher than the attention module alone, and 3.42%, 2.0%, and 10.3% higher than CNN
20 only, respectively (Figure S3). The same performances were also demonstrated in four
21 other datasets (Wheat, Foxtail millet, Rice, and Tomato). Furthermore, Cropformer has
22 comparable training time with CNN and Attention (Figures S4-7).

23 The weights of the attention mechanism can be extracted to evaluate the impact of
24 each loci on modeling decisions (Figure 1C). Based on these attention weights, loci
25 associated with crop phenotype prediction can be further identified. The entire
26 analytical framework is applicable for supporting various downstream tasks, such as
27 genomic selection and SNPs mining.

28 **Cropformer outperforms existing models for genomic prediction**

1 Five crop species (maize, wheat, foxtail millet, rice, and tomato), each with a dataset
2 of multidimensional genomic variation information, were collected from public studies.
3 We applied Cropformer to these datasets with different population sizes to assess the
4 prediction performance for both discrete (regression) and quantitative (classification)
5 traits. A range of widely used models specifically designed for crop genomic selection
6 prediction were compared, including CropGBM, DNNGP, extreme gradient boosting
7 (XGBoost), Support Vector Regression (SVR), Multilayer Perceptron (MLP), ridge
8 regression Best Linear Unbiased Prediction (rrBLUP), and Dual-extraction modelling
9 (DEM) (Supplementary Tables 2-6). We randomly divided the data of the five datasets
10 into 80% training and 20% testing sets. To avoid overfitting, we employed nested cross-
11 validation to train the model and used callback functions to guide early stopping,
12 ultimately validating the model's robustness on the test set.

13 We first trained and tested Cropformer using the maize dataset to evaluate the model's
14 performance in predicting phenotypes for days to tasselling (DTT), plant height (PH),
15 and ear weight (EW) (Figure 2A and Supplementary Tables 7-9). According to the final
16 performance evaluation of all the methods on the test dataset, Cropformer exhibited the
17 optimal performance according to PCC (DTT=92.2%%, PH=91.8%, and EW=76.3%),
18 followed by DEM, and CropGBM (DTT=89.5%, PH=88.7%, and EW=70.8%) (Figure
19 2B).

20 The performance of the compared methods on the other three datasets was also fully
21 evaluated to assess model generalizability. Cropformer achieved the best performance
22 with all the datasets. Specifically, Cropformer's performance in predicting wheat traits
23 was 63.1% for thousand kernel weight (TKW), 68.7% for grain width (GW), 66.8% for
24 grain height (GH), 49.5% for grain pressure (GP), and 72.4% for grain length (GL).
25 Cropformer outperformed CropGBM by 11.0%, 0.6%, 4.5%, 1.5%, and 1.6%,
26 respectively (Figure 3A and Supplementary Tables 10-14). As indicated in Figure 3B
27 and Supplementary Tables 15–19, analysis of the trait straw weight of the foxtail millet
28 dataset was performed using Cropformer for the regions of Anyang (83.8%), Beijing

1 (84.1%), Changzhi (86.0%), Dingxi (81.3%), and Urumqi (85.5%). These values were
2 greater than those achieved with the runner-up model (7.5%, 7.6%, 3.2%, 5.3%, and
3 6.5%, respectively) (Figure 3B and Supplementary Tables 15–19). With the rice dataset,
4 Cropformer had the best prediction performance in predictions of all five traits: 72.1%
5 for `Culm_length`, 69.5% for `days_to_heading_2018HN`, 65.5% for
6 `grain_length_width_ratio`, 72.6% for `plant_height_2018HN`, and 63.3% for
7 `thousand_grain_weight` (Figure 3C and Supplementary Tables 20–24). Compared to the
8 other methods, our model improves the prediction performance by 0.3% to 10.0%.
9 Therefore, we conclude that our approach is more effective than CropGBM, DNNGP,
10 XGBoost, SVR, MLP, rrBLUP, and DEM.

11 Furthermore, incorporating additional molecular features was feasible with the
12 Cropformer model, and here, we assessed the effect of different dimensions of
13 molecular features on the model predictions. On the tomato
14 `Sopim_BGV006775_12T001232` (an enzyme-encoding gene affecting flavonoids) trait
15 test set, Cropformer achieved PCC values of 59.3%, 64.7%, 54.7%, and 52.4% on the
16 basis of SNP, insertion and deletion (InDel), gene expression (GE), and structural
17 variation (SV) features, respectively (Figure 3D and Supplementary Tables 25–28). We
18 extracted the top 1500 weighted features from the four types of genomic variants to
19 construct fusion features. Through fusion, Cropformer achieved a prediction PCC of
20 71.5% for the `Sopim_BGV006775_12T001232` trait, which was 12.2%, 6.8%, 16.8%,
21 and 19.1% better than that achieved when using SNP, SV, InDel, and GE features,
22 respectively.

23 Finally, we benchmarked the runtime of Cropformer with other methods on five
24 datasets. In our study, CropGBM, XGBoost, SVR, MLP, and rrBLUP had the fastest
25 prediction times in small-scale (Tomato, and Foxtail millet) datasets, and Cropformer
26 was able to achieve similar time consumption. DEMs have excellent predictive
27 performance, but require longer computation times and more GPU resources. As the
28 size of the dataset increases (Maize, Rice, and Wheat), Cropformer outperforms the

1 other methods, using only a slight increase in computation time. (Figures S8A-S8E).

2 **Cropformer supports classification prediction**

3 Although the Cropformer model is a regression model for quantitative traits, it also
4 supports performing classification prediction with label-based discrete traits. To test the
5 classification performance of Cropformer, we divided DTT trait of the maize dataset
6 into three classes, samples with early flowering time (first 25% DTT), moderate
7 flowering time (25 to 75% DTT), and late flowering time (last 25% DTT), referring to
8 the method of Yan *et al* (Yan *et al.*, 2021). Moreover, we also examined performance in
9 the sample balance situation, where DTT traits were split according to early (first 50%
10 DTT) and late flowering time (last 50% DTT). We also employed the maximal
11 information coefficient (MIC) to filter out 10,000 SNPs that had high
12 representativeness. To intuitively assess the importance of the SNPs, we used Uniform
13 Manifold Approximation and Projection (UMAP) for dimension reduction and feature
14 visualization, and the results showed that the samples clustered using filtered SNPs had
15 clearer groupings than those clustered using all SNPs, suggesting that filtering can not
16 only reduce model size but also improve model performance (Figure 4A).

17 Multiple indicators were calculated for evaluating Cropformer in predicting the DTT
18 (Three-classification): the accuracy was 77.2% (Figure 4B), the precision was 77.6%,
19 the recall was 76.7%, the F1_score was 77.1% (Figure 4C and Supplementary Tables
20 30–31), and the area under the curve (AUC) was 91.2% (Figures 4D and S9). The
21 accuracy, precision, recall, and F1_score values of Cropformer were 1.7%, 0.6%, 1.7%
22 and 2.4% higher than the runner-up DEM. For the two-classification, Cropformer
23 achieved an accuracy of 83.4%, a precision of 83.8%, an overall accuracy of 83.1%, an
24 F1-score of 83.5% (Supplementary Tables 32–33), and an area under the roc curve
25 (AUC) of 90.5% (Figure 4D), outperforming the other models in prediction.

26 Next, we evaluated Cropformer's ability to handle different molecular features (SNP,
27 InDel, SV, and GE) in classification tasks. We ranked the
28 Sopim_BGV006775_12T001232 trait values in the tomato dataset and divided them

1 into three classes: class 1 (top 33% of samples), class 2 (middle 33% of samples), and
2 class 3 (bottom 34% of samples). Compared with seven other methods (CropGBM,
3 XGBoost, Support Vector Classifier (SVC), Random Forest Classifier (RFC), MLP,
4 ridge regression best linear unbiased prediction (rrBLUP), and DEM), Cropformer
5 consistently achieved the best phenotypic prediction performance on these test datasets
6 (Supplemental Tables 34-41). Based on the same processing as the regression task, we
7 extracted the 1500 most highly weighted features from the four types of genomic
8 variants to construct fusion features. In classification tasks, the fusion data-trained
9 Cropformer outperforms the single-genomic data-trained Cropformer (Supplemental
10 Tables 42-43). Particularly, our Cropformer exhibited outstanding performance,
11 outperforming the other seven methods using the fusion feature strategy.

12 **Cropformer identifies DTT-related loci by mapping of attention weights**

13 The attention weights underlying the multihead self-attention mechanism can reflect
14 the importance of each locus in phenotype prediction (Figure S10). Here, we visualized
15 the attentional weights of the loci used by the model in the training of the DTT trait
16 data (regression task) in the Manhattan plot (Figure 5A and Extended Data 1). The
17 highly ranked genes included Zm00001d029133, Zm00001d008941,
18 Zm00001d011956, Zm00001d051961 and Zm00001d025617, which are known to be
19 related to flowering time (Berr et al., 2009; Bezerra et al., 2004; Chen et al., 2017; Hong
20 et al., 2009; Kuhn et al., 2007; Liang et al., 2014; Tan et al., 2021; Zhao et al., 2005).
21 The Zm00001d008941 gene, also known as *ATX3*, has been reported to be involved in
22 flowering in maize (Chen *et al.*, 2017). A haplotype analysis of *ATX3* revealed five main
23 haplotypes in the population (Figure 5B), of which samples harbouring haplotype IV
24 exhibited the shortest DTT, which was significantly shorter than that of samples
25 harbouring other haplotypes (Figure 5C). Another gene, Zm00001d011956, is also
26 known as *SDG118* and belongs to the SET domain group (SDG) protein family. The
27 SDG family has been reported to be involved in flowering in multiple species (Berr *et*
28 *al.*, 2009; Zhao *et al.*, 2005). The haplotype analysis indicated that among the 4

1 haplotypes observed for *SDG118* (Figures 5B and E), haplotype IV exhibited a
2 significantly shorter DTT. These results indicated that Cropformer can effectively
3 capture quantitative trait loci during training, ensuring powerful predictive performance.

4 To further expand the ability of the Cropformer framework to highlight genome
5 regions with potential quantitative trait genes, an expansion module based on the
6 XGBoost algorithm (Chen and Guestrin, 2016) was developed, and the SHAP values
7 were calculated to help locate and infer candidate loci. With respect to the module,
8 locus chr8:26,168,415 and chr8:26,166,974 were among the top two according to the
9 SHAP values for the gene *ATX3*, which was consistent with the unique variations in
10 haplotype IV (Figures 5D and S11). Locus chr8:165,145,056, chr8:165,145,371, and
11 chr8:165,146,085 were highlighted on *SDG118* (Figures 5F and S12), including the
12 divergence variations between haplotypes III and IV, as well as those between
13 haplotypes I and IV. The results demonstrate that the Cropformer framework enables
14 haplotype-level analysis and assists identification of trait-related genes.

15 **Identification of loci associated with PH and EW through attention weighting**

16 Attentional weighting was then examined to mine key SNPs associated with EW and
17 PH traits in maize. We present a comprehensive list of attentional weights for SNPs
18 (Extended Data 2-3). Among the SNPs, several have already been reported, suggesting
19 the effectiveness of the list. For the maize PH trait, Zm00001d046014,
20 Zm00001d035104, Zm00001d048865, Zm00001d026791, Zm00001d047614, and
21 Zm00001d002567 were given increased attention from the Cropformer. Research has
22 revealed that Zm00001d046014, a member of the cellulose synthase-like D gene family,
23 is expressed specifically in male plants at the reproductive stage (Proost and Mutwil,
24 2018). For the EW trait, the Zm00001d038275, Zm00001d039865, Zm00001d050196,
25 Zm00001d002350, Zm00001d011367, and Zm00001d050768 played a role in
26 influencing the model's prediction. Several studies have demonstrated that
27 Zm00001d002350 functions in the synthesis of the phytohormones gibberellin and
28 terpenes (Wang et al., 2019; Wang et al., 2018b; Wang et al., 2023d). The whole list of

1 focused genes can serve as a promising reference locus for future breeding
2 improvements.

3 **Webserver for Cropformer**

4 For the convenience of scientific community, an easy-to-use webserver was established
5 to implement our Cropformer, which could be freely accessed via
6 <https://cgris.net/cropformer>. A step-by-step guide is given below. Step 1. Access the
7 website at <https://cgris.net/cropformer>, where users will find a brief overview of
8 Cropformer. Step 2. Click on the “Crop (e.g., maize)” button to access the user-selected
9 prediction module. Then, click the “Example” button to download sample data in CSV
10 format. Users can upload their own files for prediction. Step 3. Finally, click the “Run”
11 button to obtain the predicted result (Figure 6).

12 **Discussion**

13 Predicting crop traits from high-density genomic data facilitates rapid selection of
14 superior genotypes and accelerates the breeding process. As the skills and resources
15 required for genomic selection become broadly applicable, integrating interdisciplinary
16 and collaborative networks brings together different breeding programmes, offering
17 unprecedented opportunities for genomic selection research. In this study, we proposed
18 a convolution combined with a self-attention mechanism-based deep learning
19 architecture, Cropformer, to perform genome prediction utilizing both discrete traits
20 and quantitative traits. We compiled five high-quality crop benchmark datasets to
21 evaluate the predictive performance of different methods. The results demonstrated that
22 the Cropformer method outperforms other methods across the various datasets and
23 evaluation metrics and is applicable to other similar tasks (Supplementary Table 44).

24 Furthermore, Cropformer demonstrates the ability to assess the contribution of input
25 genotypes to crop phenotype prediction through the multi-head self-attention
26 mechanism at a useful resolution. In previous studies, positional information was often
27 discarded for genotype representations, such as those encoding genotypes as k-mer
28 counts or those generated via PCA for dimensionality reduction. Cropformer offers two

1 primary advantages over these methods. It employs a 0–9 encoding scheme for
2 genotype features, preserving all forms of genotypes and enabling the exploration of
3 associations between genotypes and phenotypes. With its multi-head design, the model
4 can simultaneously and independently examine multiple regions, providing a more
5 comprehensive assessment of each genotype's contribution to crop genome prediction.
6 Its attention mechanism can be used to explore the correlation between genotypes and
7 phenotypes.

8 The following limitations of our study need to be considered. First, the input to the
9 model is genotype data. Crop phenotypes result from genotype–environment
10 interactions (Fu et al., 2022; Xu et al., 2022). However, this study does not include
11 environmental data because of challenges in their collection. Incorporating suitable
12 genotypic and environmental predictors could provide new opportunities for GS.
13 Secondly, while our model helps reveal the importance of SNPs and genotypes in
14 prediction and explores their correlations, several SNPs influencing model performance
15 have been identified. However, the biological impact requires further elucidation. With
16 the advancements in high-throughput molecular biotechnology, integrating multi-omics
17 data, such as metabolomics, offers the potential to further bridge genotypes and
18 phenotypes, uncover downstream interactions, and enhance model predictive
19 performance and interpretability (Xu et al., 2024). Finally, limited data often constrain
20 the application of deep learning, especially when dealing with multimodal data (Qiu et
21 al., 2020). Even though, Cropformer achieved robust and superior performance on all
22 the test datasets.

23 In summary, Cropformer, as a general framework for crop genomic prediction,
24 provides a new algorithm option for developing superior line selection methods. With
25 Cropformer, researchers can easily perform predictive analyses on crops of interest and
26 assess the correlation of genotypes with model predictions, demonstrating the potential
27 for practical applications. We believe that Cropformer can accelerate the mining of
28 valuable gene resources for crop improvement, enhancing the progress of genomic-

1 design crop breeding and provide a valuable resource for future crop improvement
2 breeding.

3 **Methods**

4 **Dataset**

5 We analysed data from five species representing various population sizes and different
6 reproductive systems. The published datasets used in this manuscript are available from
7 websites or the literature: (1) the maize dataset(Liu et al., 2020); (2) the tomato
8 dataset(Zhou et al., 2022); (3) the rice dataset (*Oryza sativa* L.)(Wang et al., 2018a); (4)
9 the foxtail millet dataset (*Setaria italica*)(He et al., 2023); and (5) the wheat
10 dataset(Crossa et al., 2016), which can be downloaded from
11 <https://hdl.handle.net/11529/10548918>.

12 The maize dataset consisted of 1428 inbred lines derived from 24 founding female
13 crosses(Liu *et al.*, 2020). Three phenotypic traits, days to tasselling (DTT), plant height
14 (PH) and ear weight (EW), were measured in 8652 F1 hybrids at five locations. The
15 procedure for SNP calling and genotype processing of the 8652 samples has been
16 described by Liu et al(Liu et al.,
17 2020)(https://ftp.cngb.org/pub/CNSA/data3/CNP0001565/zeamap/99_MaizegoResources/01_CUBIC_related/). Furthermore, the core SNP set was screened using
18 PLINK(Purcell et al., 2007), where SNPs were removed by linkage disequilibrium
19 pruning with a window size of 1 kb, window step of 100 SNPs, and a r^2 threshold of
20 0.1, resulting in 32,519 SNPs.
21

22 We removed the samples containing missing values and finally retained 8439
23 samples. These maize samples were randomly divided into training set of 6751 samples
24 and test set of 1688 samples in a ratio of 8:2 (Supplementary Table 1, and Figure S2A).
25 To facilitate the calculation, we computed the maximum information coefficient (MIC)
26 (Wang et al., 2023a) of the SNPs in the training dataset and selected the top 10,000
27 SNPs by ranking them according to the weight of the MIC. Based on the indexing of
28 10,000 SNPs from the training dataset, the corresponding SNPs are extracted from the

1 test dataset. This ensures that the performance evaluation is objective enough.

2 The wheat dataset was derived from 2403 Iranian bread wheat (*Triticum aestivum*)
3 landrace wheat accessions in the CIMMYT wheat gene bank
4 (<https://hdl.handle.net/11529/10548918>). The dataset was genotyped for these alleles
5 using 33,709 DArT markers, with each allele recorded as 1 (present) or 0 (absent) in
6 each variety (Crossa *et al.*, 2016). For the wheat dataset, the traits measured included
7 thousand-kernel weight (TKW), grain width (GW), grain hardness (GH), grain protein
8 (GP), and grain length (GL). The same strategy was used to select the top 10,000
9 features based on the MIC, and samples containing missing values were removed,
10 resulting in 2,000 samples. These wheat samples were randomly divided into a 1600-
11 sample training set and a 400-sample testing set at a ratio of 8:2 (Supplementary Table
12 1, and Figure S2B).

13 The 3,000 Rice Genomes Project is a gigabyte dataset of genome sequences from
14 3,000 rice varieties that can represent the genetic and functional diversity of rice on a
15 global scale (Li *et al.*, 2014; Wang *et al.*, 2018a). The rice dataset includes the
16 phenotypes of five measured traits, namely, Culm_length, Days_to_heading_2018H,
17 Grain_length_width_ratio, Plant_height_2018HN, and Thousand_grain_weight
18 (https://snp-seek.irri.org/_download.zul). The 404k core SNP dataset of the rice dataset
19 was downloaded from https://snpseek.irri.org/_download.zul, and the top 10,000 SNPs
20 were selected based on the MIC. The same strategy was applied to remove missing
21 values and the segmented rice dataset, resulting in 2799 samples, a training set
22 containing 2239 samples and a testing set containing 560 samples (Supplementary
23 Table 1, and Figure S2C).

24 In the foxtail millet dataset, 680 foxtail millet accessions from 13 different
25 geographic locations were sequenced by He *et al.* (He *et al.*, 2023)
26 (<https://www.cgris.net/millet>). This dataset includes the phenotypes of five measured
27 traits, namely, straw weight (Anyang), straw weight (Beijing), straw weight (Changzhi),
28 straw weight (Dingxi), and straw weight (Urumqi). We used the high-effect marker

1 SNPs identified by He et al.(He *et al.*, 2023). as feature inputs to the model and obtained
2 666 samples after removing missing values. These foxtail millet samples were
3 randomly divided into a 566-sample training set and a 100-sample testing set at a ratio
4 of 8:2 (Supplementary Table 1, and Figure S2D).

5 The tomato dataset was a call set (designated TGG1.1–332) from the tomato graph
6 pangenome consisting of 6,971,059 SNPs, 657,549 InDels, 51,155 GEs, and 54,838
7 SVs(Zhou, 2022) (<http://solomics.agis.org.cn/tomato/ftp/genotypes/>). An important
8 traits (Sopim_BGV006775_12T001232) associated with tomato yield and flavor were
9 used for study and analysis. We pruned the SNPs, InDels, and SVs(Zhou, 2022) using
10 PLINK and MIC to obtain the top 10,000 features and removed phenotypes containing
11 missing values, resulting in 332 samples. These tomato samples were randomly divided
12 into a 265-sample training set and a 67-sample testing set at a ratio of 8:2
13 (Supplementary Table 1, and Figure S2E).

14 During the data splitting process, we set a random seed. The introduction of a
15 random seed ensures that there are no specific patterns or correlations between different
16 parts of the dataset, thereby making the resulting training and testing sets representative
17 and accurately assessing the model's generalization ability. This approach also ensures
18 that the data splitting procedure remains uniform across different traits, facilitating fair
19 and reliable comparisons of multi-trait predictability. We applied MIC analysis to the
20 maize, wheat, and tomato datasets, selecting the top 10,000 features based on their
21 importance ranking. For the foxtail millet (*Setaria italica*) and rice datasets, we utilized
22 the core SNPs provided by He et al.(He *et al.*, 2023) and Liu et al.(Wang *et al.*, 2018a),
23 as the feature dimensions did not exceed 10,000, and thus, further MIC processing was
24 not performed.

25 **Feature representations for genotypic data**

26 For ease of inputting the data into the model and interpreting the features, we coded the
27 SNP information using 0–9 as follows: AA (0), AT (1), TA (1), AC (2), CA (2), AG (3),
28 GA (3), TT (4), TC (5), CT (5), TG (6), GT (6), CC (7), CG (8), GC (8), and GG (9).

1 For the InDel and SV information, we used PLINK to encode them as 0, 1, or 2. For all
 2 models, we use the same feature representation scheme to train and test to ensure
 3 fairness of comparison. For different gene variants, we extracted the top 1500 MIC
 4 weighted features and vertically merged them to train the models.

5 **MIC**

6 The core idea of MIC is: if there is a relationship between two variables, there will be
 7 a grid that can split the scatter graph of the two variables to encapsulate this relationship,
 8 and then normalize these mutual information values to ensure a fair comparison
 9 between grids of different dimensions (Albanese et al., 2013; Reshef et al., 2011; Zhou
 10 et al., 2004)

$$11 \quad I(X; Y) = \sum_{x,y} p(x,y) \log \frac{p(x,y)}{p(x)p(y)} = H(X) - H(X|Y)$$

12 Where $\|x - c_i\|$ represents Euclidean norm; c_i , R_i and σ_i are the center, the width
 13 and the output of the i_{th} hidden unit, respectively.

14 **Cropformer architecture**

15 We introduce Cropformer, a hybrid network based on a convolutional neural network
 16 (CNN) combined with a multihead self-attention mechanism that accurately predicts
 17 the phenotypic performance of plants from their genome features. The model accepts
 18 sequence information of variable lengths. To utilize the mini-batch technique for
 19 training and prediction, we fix the length of the input sequence at 10,000 nt. We
 20 employed the Maximum Information Coefficient (MIC) method to identify the top
 21 10,000 SNPs with high weights that are closely associated with the phenotype.
 22 Specifically, the data pass through a convolutional layer that employs a kernel size of
 23 3×3 , with a stride (step size) of one and padding set to one. This configuration is
 24 designed to ensure that the dimensionality of the output matches that of the input.

25 The core component of our network is a multihead self-attention layer. The multi-
 26 head self-attention mechanism is used to assess the contribution of sequence regions

1 for localization by multiple heads (head = 8), which has the ability to further detect
 2 localization SNPs during the prediction. We borrow the idea proposed by Bengio et
 3 al.(Zhouhan Lin et al., 2017) that the overall semantics of a sentence are composed of
 4 multiple constituents and that a multihead self-attention mechanism can be used to
 5 address different parts of the sentence. Attention can model the dependence of CNN-
 6 fed data regardless of their distance, a property we use to capture core SNPs. The
 7 attention matrix of self-attention can be obtained by computing the vectors Query (Q),
 8 Key (K) and Value (V). The input of the attention layer and its two linear transformations,
 9 Q and K, are defined as follows(Ullah and Ben-Hur, 2021):

$$10 \quad Q = W_Q^T X$$

$$11 \quad K = W_K^T X$$

12 where W_Q and W_K are the corresponding weight matrices for Q and K, respectively.

13 The attention matrix A is then computed using the following expression:

$$14 \quad A(Q, K) = \text{softmax}\left(\frac{QK^T}{\sqrt{d_k}}\right)$$

15 where d_k is the dimension of K. The SoftMax function is applied to each row of the
 16 matrix $\frac{QK^T}{\sqrt{d_k}}$, ensuring that the elements of each row sum to 1.

17 To generate the output of the attention layer, we define the value matrix:

$$18 \quad V = W_V^T X$$

19 Finally, we define the output of the attention layer as follows:

$$20 \quad Z = A \times V$$

21 Next, we perform a linear transformation of the reshaped data, introduce dropou
 22 and normalize the output, which is effective in terms of computational efficiency and
 23 leads to better model accuracy. To avoid overfitting, we used early stopping in
 24 Cropformer. Finally, for continuous traits, we use the mean square error to define the
 25 loss function, and for qualitative traits, we define the loss function using CrossEntropy.

26 **Attention weights**

27 In practical terms, the self-attention mechanism allowed the inputs to interact with

1 themselves and determined which element should receive more attention(Liu et al.,
 2 2023b). The attention mechanism was described as mapping a query and a set of key–
 3 value pairs to an output, where the query, keys, values, and output were all vectors. We
 4 used the excellent data feature extraction potential of CNNs to process encoded
 5 genotype data without changing the length of the sequence(Garcia-Gasulla et al., 2018).
 6 The output of the CNN was the same length as the input data, so we could calculate the
 7 overall attention weights and generate an attention vector for each input(Yan et al.,
 8 2022). For each dimension, the attention score indicated the importance of the
 9 dimension for model prediction.

10 In this study, we employed the dynamic weight allocation mechanism to capture
 11 attention scores. Specifically, each attention head's output was weighted according to
 12 its importance score (Head Importance Score), which was dynamically updated
 13 throughout the training. This mechanism ensured that attention heads contributing more
 14 significantly to the task received higher weights, thereby preventing the loss of critical
 15 information. During training, the importance score of each attention head was learned
 16 adaptively, allowing the model to adjust the contribution of each attention head
 17 according to its relevance to the task. The final output was a weighted combination of
 18 each attention head, where attention heads with higher importance scores contributed
 19 more. To ensure the output of each attention head was appropriately scaled before
 20 merging, we normalized the importance scores, defined as:

$$21 \quad \alpha_i = \frac{S_i}{\sum_{j=1}^N S_j}$$

22 where α_i is the weight for the i -th attention head, and S_i is its importance score.

23 **Multimodal data integration**

24 Advances in next-generation sequencing technologies have led to a proliferation of
 25 multimodal datasets. The multimodal data, including SNP, InDel, GE, and SV, from
 26 332 tomato samples were used for further analysis. For the SNP data, we employed a
 27 0–9 coding scheme, the details of which are provided in “Feature representations for

1 genotypic". With respect to the InDel and SV information, we utilized PLINK to encode
2 them as 0, 1, or 2. For each modality, we adopt columnwise concatenation to construct
3 fused features for model training.

4 **Clustering**

5 The StandardScaler function of scikit-learn (version: 1.5.1) was used by us to normalize
6 the three-classification data and the two-classification dataset respectively. We use
7 matplotlib for the visualization (version: 3.7.5). The python package umap-learn
8 version 0.5.3 was used for UMAP visualization.

9 **Haplotype analysis**

10 We performed haplotype analysis and generated haplotype networks with Pegas 0.11
11 (Paradis, 2010) in R. We utilized the ggplot2, gghalves, and ggpubr packages in R to
12 generate boxplots of the DTT trait with at test for different haplotypes. For the gene
13 structure plot, annotation information for the Zm00001d008941_T001 transcript was
14 first extracted from the GFF file (B73, v4.48); subsequently, the three_prime_UTR and
15 five_prime_UTR were plotted as white-filled rectangles, while the CDS features were
16 plotted as red-filled rectangles. The length and relative position of those rectangles
17 follow their physical positions. The physical positions of the various loci were mapped
18 to the gene structure and are marked as red vertical lines. For the genotype heatmap of
19 haplotypes, the consensus genotype for each haplotype at each mutation locus was
20 defined as the genotype with the highest frequency at that locus within the population
21 corresponding to the haplotype, and the consensus genotypes were then plotted in
22 different colours (grey, light blue, and dark blue for the reference genotype,
23 heterozygous mutation, and homozygous mutation, respectively). The gene structure
24 plot and the genotype heatmap of Zm00001d011956 were generated in the same way.

25 **SHapley Additive exPlanations**

26 SHAP (SHapley Additive exPlanations) is a commonly used explanatory machine
27 learning model that shows the magnitude of the overall contribution of features to the
28 prediction of the the whole dataset(Lundberg and Lee, 2017; Qiu et al., 2022; Tang et

1 al., 2023). Based on the highly weighted SNPs extracted by the self-attention
 2 mechanism, we annotated them and selected genes Zm00001d011956 and
 3 Zm00001d008941 associated with flowering time. For the locus of both genes, we
 4 searched for SNPs within an extended region of 400 kbp (half the LD length). We use
 5 Explainer, which provides a localized explanation of the impact of input SNPs on the
 6 individual predictions of the XGBoost model. Here, a higher SHAP value means more
 7 weight.

8 **Evaluation metrics**

9 We use five outer and three inner nested cross-validation to partition the training
 10 datasets(Cawley and Talbot, 2010). The inner layer cross-validation is used for
 11 hyperparameter optimization and outer layer cross-validation is used to evaluate the
 12 generalization performance of the model. Finally, the robustness of the model is
 13 evaluated on the test datasets. For qualitative traits, accuracy, recall, precision, and
 14 F1_score metrics were used to quantify the performance of the model and are defined
 15 as follows(Liu et al., 2023a; Wang et al., 2021; Wang et al., 2023c):

$$16 \quad \text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN}$$

$$17 \quad \text{Recall} = \frac{TP}{TP + FN}$$

$$18 \quad \text{Precision} = \frac{TP}{TP + FP}$$

$$19 \quad \text{F1_score} = \frac{2 * (\text{precision} * \text{recall})}{\text{precision} + \text{recall}}$$

20 where TP, TN, FP, and FN represent the numbers of true positives, true negatives,
 21 false-positives, and false-negatives, respectively.

22 The AUC is an indicator of a classification model's performance, representing its
 23 ability to classify at varying thresholds. It evaluates the classification effect of the model
 24 by calculating the area under the ROC curve, and the closer the AUC value is to 1, the
 25 better the classification performance of the model. The Pearson correlation coefficient
 26 is used to assess the predictive performance of the model in continuous trait tasks by
 27 measuring the linear relationship between true and predicted values. A coefficient closer
 28 to 1 indicates a higher predictive accuracy of the model.

Data availability and Code availability

Some of the data that support the findings of this study are publicly available, and some are proprietary datasets provided for this analysis under collaboration agreements. The raw whole genome sequencing of maize is available at NCBI under BioProject Accession No. PRJNA597703. Rice sequencing data are available through NCBI under project accession number PRJEB6180. The tomato dataset can be found in the SolOmics database (<http://solomics.agis.org.cn/tomato/ftp>). The wheat dataset can be found on the website (<https://hdl.handle.net/11529/10548918>). The foxtail millet dataset can be found at this link (<https://www.cgris.net/millet>). The Cropformer software including documents and tutorial is available on Github (<https://github.com/jiekese/Cropformer>).

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Contributions

H.W., S.Y., W.X.W., W.F., W.L.G., and Y.Q.C. designed this study and wrote the paper. H.W. built the deep learning models. W.X.W., Y.M.C, J.P.H., and Y.Q.C. processed and analyzed the data. H.W., Q.H., and X.M.D. collected the dataset and performed data preprocessing. Y.N.L., Y.S.C., and Y.Q.C., conceived the project and edited the paper.

All authors reviewed and approved the final manuscript for submission.

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1 **Competing interests**

2 The authors declare no competing interests.

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19 Figures

20
 21 **Figure 1.** Workflow of the proposed Cropformer framework. **A** We collected genotype
 22 information for five crops. Then, we convert the genotype information into a "one-hot
 23 code" representation and input it into the neural network for trait prediction. **B** The
 24 Cropformer model mainly consists of CNN filters and a multihead self-attention layer.
 25 The CNN layer is used to capture the localization signals of SNPs, and multihead self-
 26 attention is used to make the model more focused on important SNPs. **C** From left to
 27 right, the sequence shows the results of haplotype analysis, attention weight
 28 visualization, feature importance assessment (SHapley Additive exPlanations (SHAP)
 29 based explanation of machine learning model outputs.), and clustering analysis.

1 **Figure 2.** Predictive performance of the Cropformer model on mvvaize data (Train and
2 Test datasets, regression task). **A** The phenotypic distributions of ear weight (EW), plant
3 height (PH), and days to tasselling (DTT) of the maize dataset in the training and test
4 datasets. **B** Comparison of predictive performance of different models on DTT, PH and
5 EW traits in maize for training set (nested cross-validation) and test set. These models
6 include our model, the CropGBM, the DNNGP, XGBoost, SVR, MLP, rrBLUP, and
7 DEM. Model performance was measured using Pearson correlation coefficient.

8

9 **Figure 3.** The predictive performance of the Cropformer model on the test datasets of
10 wheat, foxtail millet, rice and tomato (continuous traits, regression task). **A** The
11 predictive performance of different algorithms for five traits, namely, thousand-kernel
12 weight (TKW), grain width (GW), grain hardness (GH), grain protein (GP), and grain
13 length (GL), on the wheat dataset. **B** The prediction performance of different algorithms
14 on the foxtail millet dataset was compared for the straw weight trait from five regions,
15 namely, Anyang, Beijing, Changzhi, Dingxi, and Urumqi. **C** Predictive performance for
16 five traits, Culm_length, Days_to_heading_2018H, Grain_length_width_ratio,
17 Plant_height_2018HN, and Thousand_grain_weight, on the rice dataset according to
18 the different algorithms. **D** Based on the genomic variation information, including
19 single nucleotide polymorphism (SNP), insertion deletion (InDel), gene expression
20 (GE), structural variation (SV), and the fusion of these four types of information, we
21 compared the modelling performance of different algorithms for the
22 Sopim_BGV006775_12T001232 trait in the tomato dataset.

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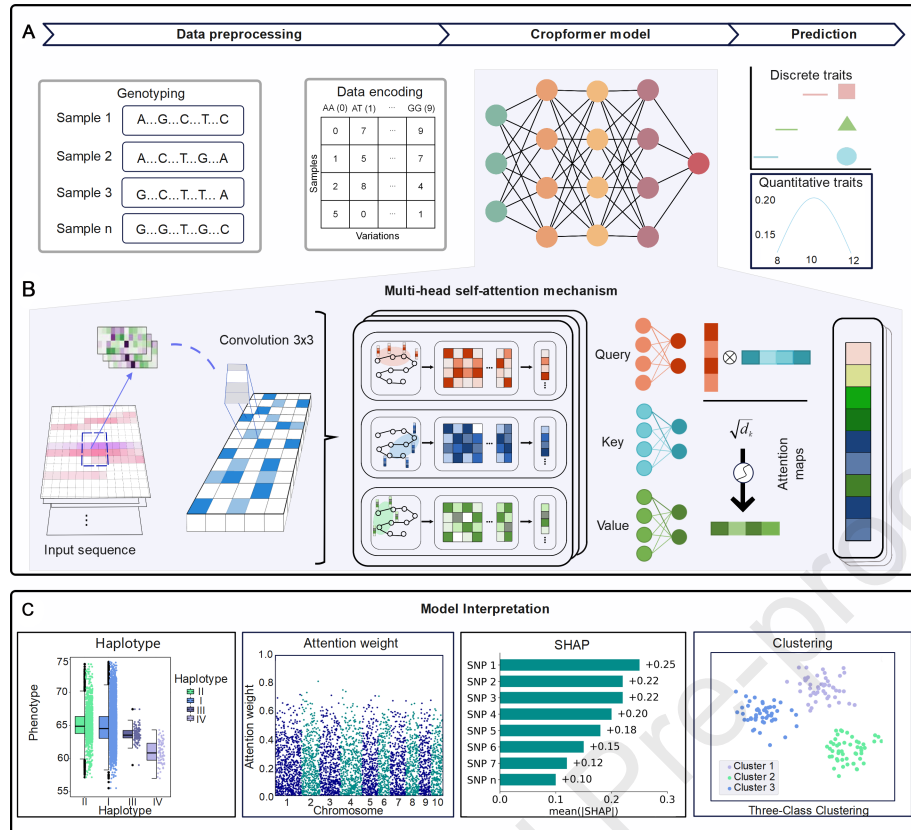
2 **Figure 4.** Classification prediction performance of the Cropformer model on the maize
3 dataset (10,000 SNPs, classification task). **A** UMAP visualization of all the SNPs and
4 the 10,000 SNPs extracted from the MIC. From left to right, there are three
5 classifications and two classifications. **B** Comparison of the accuracy of different
6 models on the maize training (nested cross-validation) and test datasets. **C**
7 Comprehensive predictive evaluation of the Cropformer model on a maize test dataset
8 with five metrics: Accuracy, Precision, Recall, F1_score, and Area under the curve
9 (AUC). **D** Comparison of different models for classification of early flowering time
10 (first 25% DTT), moderate flowering time (25 to 75% DTT) and late flowering time
11 (last 25% DTT) DTT based on 10,000 SNPs. The numbers in brackets are AUC values.

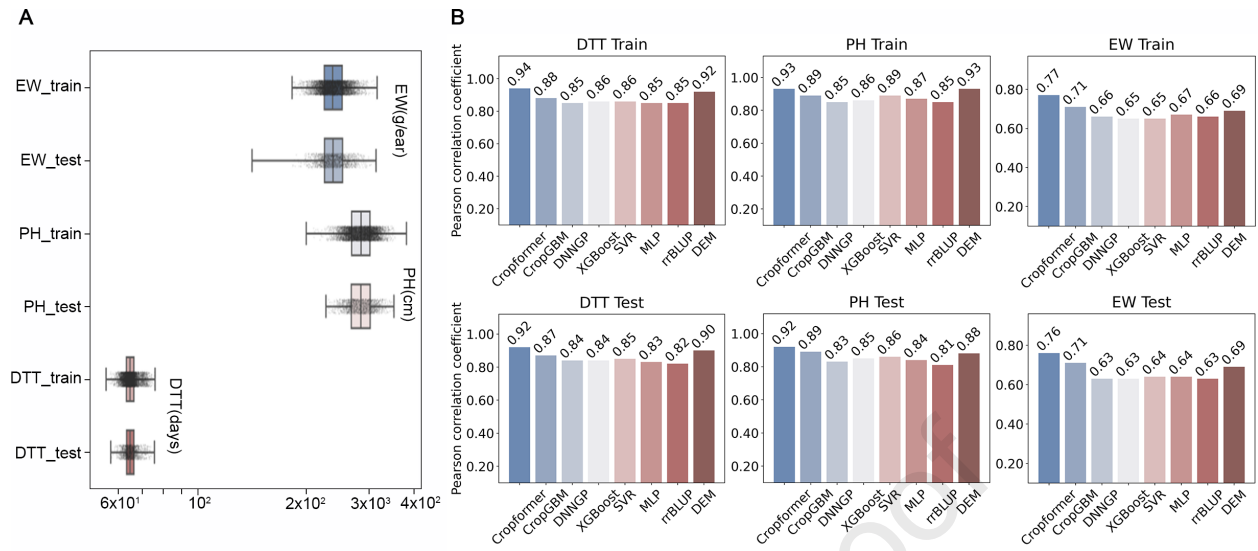
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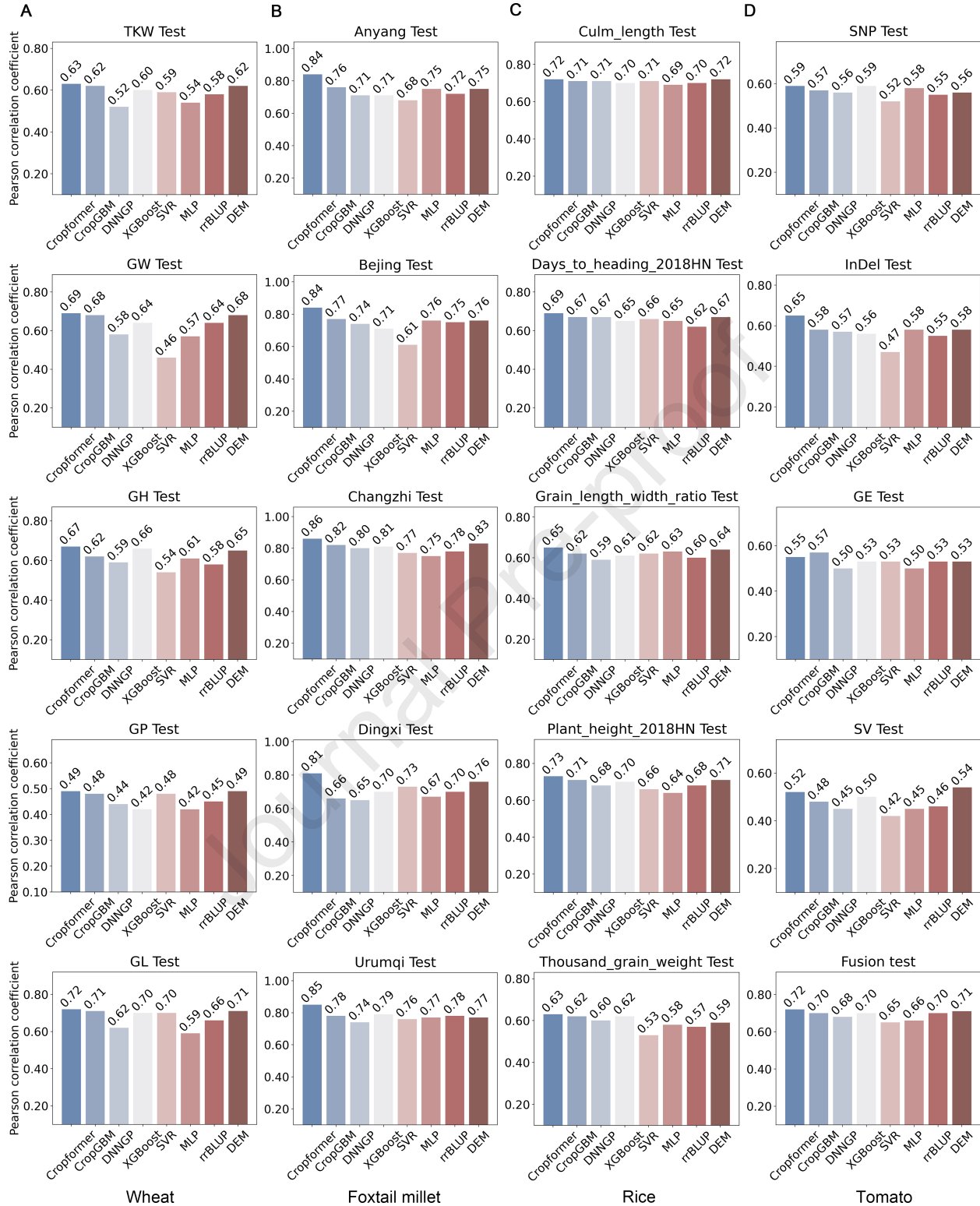
13 **Figure 5.** Cropformer can infer the contribution of SNPs to GS (Regression task). **A**
14 Mapping of attentional weights to SNPs for maize DTT traits (Regression). The x-axis
15 represents the SNP index position; the y-axis represents attentional weights (Only SNPs
16 with attention weights greater than 1 are shown). **B** Comparison of traits among
17 haplotypes. DTT comparisons among accessions harbouring different haplotypes of
18 Zm00001d008941 and Zm00001d011956. **C** Haplotype network of Zm00001d008941.
19 Circles represent haplotypes, and haplotypes are linked to their most similar relatives.
20 Short lines indicate the diversity between linked haplotypes. **D** Gene structure and
21 haplotypes of Zm00001d008941 in maize. The consensus genotype of each haplotype
22 is marked in grey, light blue, and dark blue for the reference genotype, heterozygous
23 mutation, and homozygous mutation, respectively. The purple bar graph represents the
24 feature importance analysis based on XGBoost (Regression). **E** Haplotype network of
25 Zm00001d011956. **F** Gene structure and haplotypes of Zm00001d011956 in maize. The
26 purple bar graph represents the feature importance analysis based on XGBoost
27 (Regression)

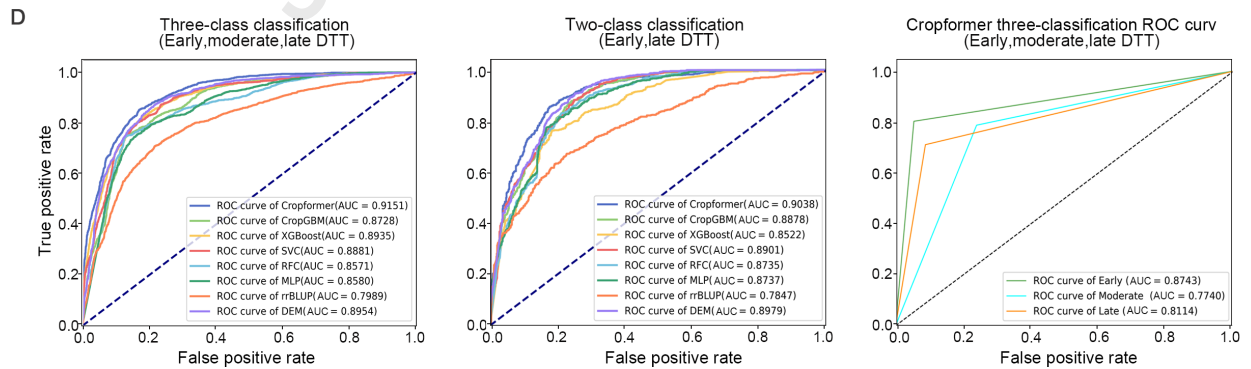
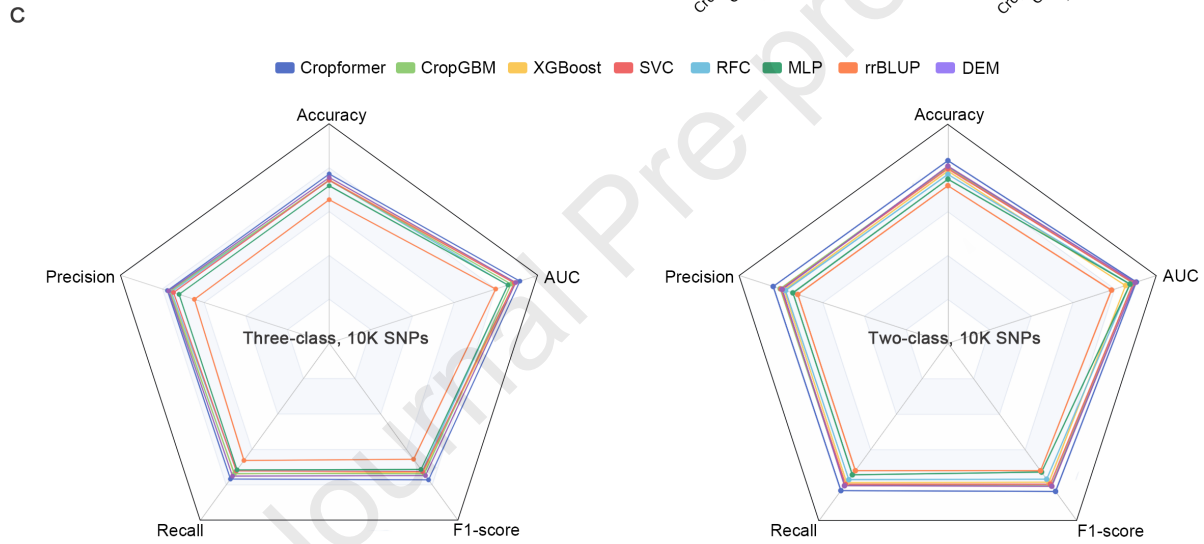
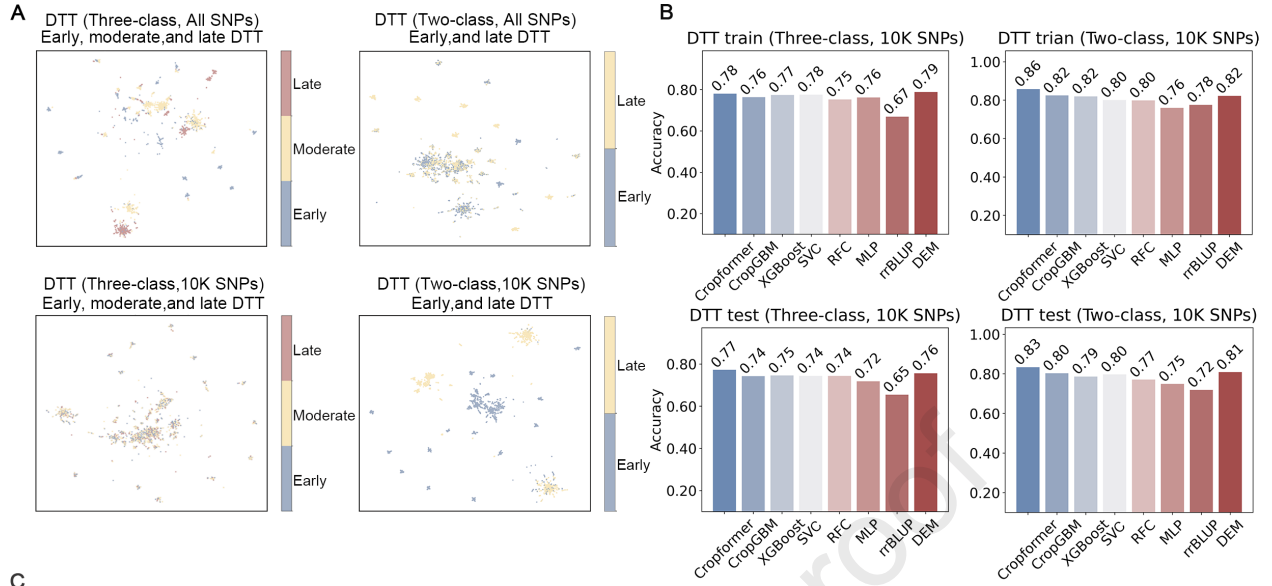
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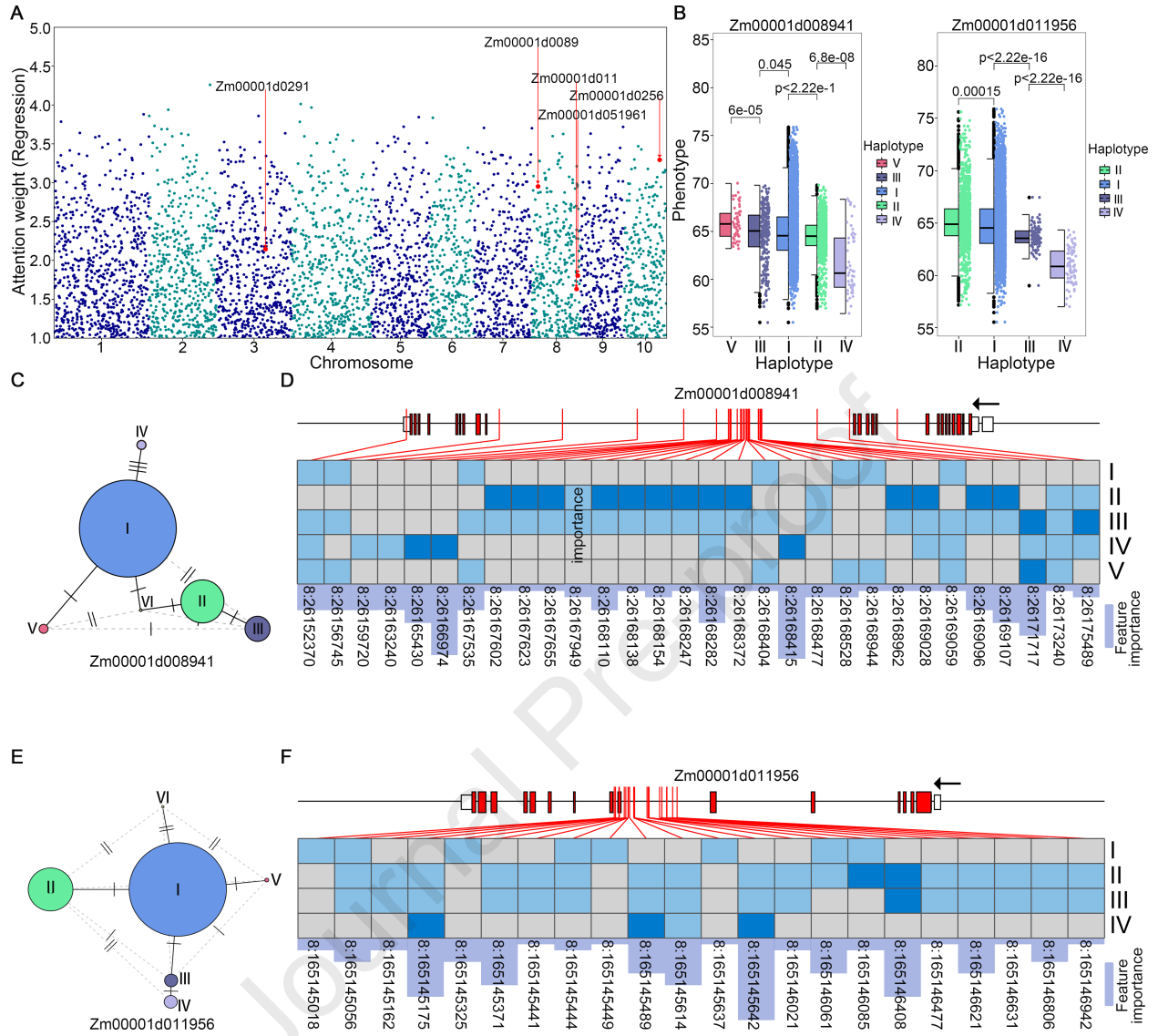
29 **Figure 6.** Cropformer web server.











Cropformer

Crop Genome Prediction

Home Rice ▾ Maize ▾ Wheat ▾ Millet ▾ Tomato ▾ About

Welcome to Cropformer

Machine learning and deep learning have been employed in genomic selection (GS) to expedite the identification of superior genotypes and accelerate breeding cycles. However, a significant challenge for current data-driven deep learning models in GS is the low robustness and lack of interpretability. To address this challenge, we developed Cropformer, a deep learning framework for predicting crop phenotypes and exploring downstream tasks. The framework consists of a combination of convolutional neural networks and multiple self-attention mechanisms for better accuracy and interpretability. Here, Cropformer prediction of complex phenotypic traits is extensively evaluated for more than 20 traits across five main crops, namely, maize, rice, wheat, foxtail millet, and tomato, demonstrating significant improvements in both precision and robustness over the performance of state-of-the-art GS methods. Compared to the runner-up model, Cropformer's prediction accuracy improved by up to 7%. Here, we provide an online webserver where users can directly upload their files for prediction. Please see the About board for the detailed format.

20 Oct 2024: Cropformer is now open!



Rice



Maize



Wheat



Millet



Tomato



14 (77x) visits
REVOLVERMAPS