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Genomic analyses reveal a lack of widespread strong selection in indigenous chickens

Zilong Wen [a,1], Xinyu Cai [a,1], Zexuan Liu [a], Lizhi Tan [a], Yuan Kong [a], Yuzhan Wang [a], Yiqiang Zhao [a,b,*]

[a] State Key Laboratory of Animal Biotech Breeding, College of Biological Sciences, China Agricultural University, Beijing 100193, China
[b] National Research Facility for Phenotypic and Genotypic Analysis of Model Animals (Beijing), China Agricultural University, Beijing 100193, China

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ABSTRACT

The study of domestication has been revolutionized with the advent of molecular genetics. Chickens, with their clear domestication history, emerge as an excellent model for study into the paths of evolution in domestication and improvement. Here we used genomic data from wild, indigenous, and commercial chickens to better understand how genetic drift and selection translate into their differentiations. Our investigation into the patterns of allelic change and divergence reveals a polygenic architecture governing genetic differentiation during domestication and improvement. We uncover distinctive population-specific differentiations in terms of genes and functions among wild, indigenous, and commercial chickens. Using Runs Of Homozygosity (ROH) based mixed model approach developed in this study, we identified only directional selection signatures occurring in wild and commercial chickens. Notably, our findings suggest that indigenous chickens serve as reservoirs of genetic diversity, necessary for rapid adaptation to new environments or subsequent modern breeding. This work provides unprecedented insights into the chicken domestication and improvement, and it illuminates our understanding of the domestication of other animal species.

Introduction

Animal domestication is the process of adapting animals from a wild state to a domesticated one, driven by human needs (Gamble et al., 2004; Larson and Burger, 2013; Larson et al., 2014; Larson and Fuller, 2014; Zeder, 2015). The modern chicken (*Gallus gallus domesticus*) was domesticated at least 4000-4500 years ago in Southeast Asia from the Red Junglefowl (RJF) (Liu et al., 2006; Wang et al., 2020; Lawal et al., 2020; Hata et al., 2021), and underwent two distinct processes of domestication and improvement (Zhou et al., 2018; Lawal et al., 2018; Qanbari et al., 2019; Zhang et al., 2022; Yang et al., 2022). As a result, there are now over 1000 breeds of indigenous chickens (https://www.fao.org/poultry-production-products/production/poultry-species/chickens/en/), as well as specialized breeds for commercial purposes such as meat (broilers) and egg (layers) production.

Previous studies, by evaluating polymorphic levels within populations and comparing allelic frequencies between wild and commercial chicken populations, have identified loci exhibiting significant selective sweeps in modern broilers and layers. This serves as empirical evidence for domestication and artificial selection (Rubin et al., 2010; Qanbari et al., 2019). However, it is important to note that selective breeding for commercial chickens has only occurred in the last 200 years, genetic analyses that overlook indigenous chickens could lead to oversimplification of patterns and details of genetic change in the chicken genome. As an essential intermediate step towards specialized commercial breeding, a joint investigation into the genomic architecture of indigenous chickens would enhance our understanding of the genetic foundation and comprehensive processes of domestication and improvement (Zhou et al., 2018; Zhang et al., 2022; Lan et al., 2024).

In this study, we conducted a comprehensive analysis of genetic change and coherence selection throughout chicken domestication and improvement based on the whole-genome data of wild, indigenous and commercial chickens. Our study made two significant advances in the understanding of chicken domestication. First, we unveiled the absence

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* Corresponding author at: State Key Laboratory of Animal Biotech Breeding, College of Biological Sciences, China Agricultural University, Beijing 100193, China.
E-mail address: yiqiangz@cau.edu.cn (Y. Zhao).

[1] These first two authors contributed equally to this work.

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of extensive genetic differentiation in either domestication or improvement. The global genetic differentiation is consistent with a polygenic architecture, where the cumulative effects of numerous minor changes contribute to the differentiation among wild, indigenous and commercial chickens. Second, by employing the ROH modeling approach, we pinpoint credible but limited signatures of directional selection and identify genes under selection for chickens at wild and commercial stages. By examining the genetic architecture of indigenous chickens, we reveal that genome evolution is predominantly shaped by random drift. We propose that the relaxed selection in indigenous chickens enhances the prevalence of genetic diversity, thereby facilitating the transition from the wild status to subsequent commercial breeding. This study contributes to advancing our comprehension of the genetics of chicken domestication and improvement. Furthermore, the insights gained here offer valuable perspectives for investigating the domestication processes of other animals.

Materials and methods

Genetic materials

We compiled a published Illumina chicken 60 K single nucleotide polymorphisms (SNPs) genotyping data of 1,028 samples from 13 chicken breeds (Zhang et al., 2019b). Of the samples used herein, they include seven Chinese indigenous breeds of 79 Beijing Fatty (BF), 83 Huiyang Bearded (HY), 74 Jinhu Black-Bone (JH), 89 LangShan (LS), 90 QingYuan (QY), 75 Silkie (SK) and 95 WenChang (WC) chickens; 2 commercial breeds, including 180 White Plymouth Rock (WPR) and 54 White Leghorns (WL) chickens. And 4 wild-type populations, including 4 Red Junglefowl (RJF), 71 Tibetan (ZJ), 46 DeHong (DH) and 88 ChaHua (CH) chickens. This is consistent with the phylogenetic tree results from (Wang et al., 2020), which indicate that RJF is most closely related to indigenous chickens from Yunnan and Tibet, China. The geographic distribution of chickens is shown in Fig. S1 and the sample details are listed in Table S1.

Data preparation

The SNPs with minor allele frequency (MAF) < 0.05 or call rate $<$ 95% across all samples were excluded. SNPs were pruned by the PLINK v1.9 (Purcell et al., 2007) using a threshold of pairwise $r^2 = 0.2$ within 50 SNP sliding windows with a step of five SNPs across the genome. Following the release of the newest reference genome GRCg6a, we converted the Galgal 5.0 (Groenen et al., 2011) coordinates to the corresponding the GRCg6a coordinates. This transformation was executed utilizing an in-house script, based on the European Variation Archive (EVA) (Cezard et al., 2022) database, where duplicates and loci no longer present in the updated EVA database were deleted. We kept only bi-allelic SNPs on autosomes in the final dataset of 45,749 SNPs from 1,028 samples for subsequent analyses.

Population structure analysis

Principal component analysis (PCA) was performed on the 45,749 qualified SNPs of 1,028 samples using the PLINK v1.9. To assess the quality of clustering, the Silhouette score was calculated based on the first two principal components (PCs). The 'metrics.silhouette_score()' function from the scikit-learn-v0.24.2 Python package (Peng et al., 2022) was used for this purpose. In this study, the clustering refers to the classification of chickens belonging to wild, indigenous, and commercial stages.

The pairwise identical-by-state (IBS) distances between individuals were computed using the PLINK v1.9. Unrooted neighbor-joining (NJ) tree was constructed using the distance matrix with FastME-2.0 (Lefort et al., 2015) (-D 1 -b 1000 -B -m N -s –I) and was visualized using ggtree (Yu et al., 2017).

Outgroup f_3-statistics

The outgroup f_3-statistics (Raghavan et al., 2014) were employed to assess the population similarity by measuring the shared drift between populations, through the topology *f*3(population A, population B; outgroup). The f_3 function in the admixr (Petr et al., 2019) was used to compute outgroup *f*3-statistics. A higher *f*3 value serves as an indicator of a higher genetic affinity between population A and population B.

Genetic diversity and differentiation

The VCFtools-v0.1.16 (Danecek et al., 2011) was used to calculate nucleotide diversity (Pi) and the LASSI-Plus (DeGiorgio and Szpiech, 2022) was used to calculate haplotype H12 statistic for genomic windows. A lower H12 value indicates a higher haplotype diversity. To measure genetic differentiation, fixation index (F_{ST}) values were calculated for genomic windows across the two evolutionary stages, specifically for domestication (from wild chickens to indigenous chickens) and for improvement (from indigenous chickens to commercial chickens) using the VCFtools.

The degree of linkage disequilibrium (LD) decay was assessed by measuring the correlation (r^2) for all pairs of SNPs within 1000 kb using the PopLDdecay v3.41 (Zhang et al., 2019a). Across all samples, the median distance for LD persistence of $r^2 = 0.1$ was approximately 200 kb (Fig. S2). Therefore, a window size of 200 kb was adopted for all analyses unless otherwise specified.

Tajima's D values were calculated separately for wild, indigenous, and commercial chickens using VCFtools v0.1.16 with the parameter "-TajimaD 200000", which applies a 200 kb window size for the calculation. The average Tajima's D value was then computed across all windows for each population.

Decomposition of population differentiation

The Gaussian Mixture Model (GMM) is a probabilistic model that assumes observed data points originate from a mixture of Gaussian distributions, each characterized by its own mean, variance, and weight parameters. The 'Mclust()' function in the mclust-v6.0.0 R package was used to fit the GMM model for the decomposition of F_{ST} calculated in chicken domestication and improvement, respectively. The Bayesian information criteria (BIC) was used to compare different models and select the one that best fits the data.

Analysis of polygenic architecture of genetic differentiation

To understand the polygenic architecture of genetic differentiation, we fitted all SNPs simultaneously in one model to estimate the proportion of variance explained (PVE). The model is as follows:

$$logit(p) = X\beta + g_1 + g_2 + g_3 + g_4 + e$$

where Y represents the two evolutionary stages from domestication or improvement, as described above. Here, $p = P(Y = \text{lower stage} \mid X, g)$ (the lower stage denotes the wild stage for domestication or the indigenous stage for improvement) is the probability to be modeled; X is the first 10 PCs included as fixed-effect covariates; β is the vector of regression coefficients; g is the polygenic random effect (i.e., the accumulated effect of SNPs as captured by the genetic relationship matrix (GRM)), and e is the model residual. According to the GMM estimation, we split all SNPs into four sets and used GCTA (Yang et al., 2011a) to compute a GRM for each set. The PVE was calculated as:

$$PVE = \frac{V_{g1} + V_{g2} + V_{g3} + V_{g4}}{V_{g1} + V_{g2} + V_{g3} + V_{g4} + V_e}$$

where Vg is the variance of the polygenic random effect and Ve is the variance of the residual. The process of modelling and variance

component estimation were performed using the MTG2 (Lee and Van Der Werf, 2016) software.

If the genetic differentiation is polygenic, the PVE by each chromosome is expected to be correlated with the sizes of individual chromosomes. We tested this by estimating the PVE for each chromosome and then correlating the PVE with individual chromosomes sizes. This analysis was performed for both chicken domestication and improvement.

LSBL analysis for population-specific differentiation

Based on pairwise F_{ST} distances, locus-specific branch length (LSBL) identifies population-specific differentiation by considering a predefined trifurcating tree. Taking population A as an example, its LSBL statistic was calculated for each genomic window across three populations as follows:

$$LSBL(A) = \frac{d_{AB} + d_{AC} - d_{BC}}{2}$$

where dAB, dAC, and dBC are the F_{ST} distances between pairs of three populations of A, B, and C, while LSBL(a) assesses the directional differentiation of population A.

We computed LSBL statistics for wild, indigenous and commercial chickens separately using a 200-kb non-overlapping sliding window. The *Z*-transformation of LSBL statistics was produced and subsequently converted into *P*-value using cumulative probability. Specifically, a *Z*-score greater than 1.96 was deemed indicative of significance ($P < 0.05$), while a *Z*-score surpassing 2.56 was considered highly significant ($P < 0.01$). RJFs were excluded from the LSBL analysis due to their limited sample size.

ROH-based selection model

The Runs Of Homozygosity (ROH) are contiguous homozygous segments commonly employed for estimating genetic diversity and detecting signatures of selection. The detectRUNS (Biscarini, 2019) R package was used to identify ROH for each sample with default settings. The proportion of ROH in a 200-kb genome window was then calculated using the BEDtools (Quinlan and Hall, 2010). As the window-based ROH-ratio approximated a discrete 0-1 distribution, we applied a hard threshold of 0.5 to dichotomize the window into binary states {0, 1} (Fig. S3).

Under the rationale that selection results in a higher probability of finding ROH segments within a population, for each window, we associated the individual-level ROH state with the evolutionary stages using a generalized linear mixed model. This was accomplished through the glmer function in the lmerTest (Kuznetsova et al., 2017) R package as follows:

$$logit(p) = X\beta + u + e$$

where Y represents a binary variable indicating the focal window to be a ROH or not {0, 1}. Here, p = P (Y = 1 | X, u) is the probability to be modeled; X is the indicator variable for evolutionary stages as fixed effect, β is the vector of fixed effect to be tested for association; u is the random intercept to adjust effects of breeds within the same evolutionary stages, and e is the model residual. To control false positives, we used the false discovery rate (FDR) method for *P*-value correction.

It is noteworthy that the three evolutionary stages could be coded either categorically or ordinally. The utilization of categorical coding {wild, indigenous, commercial} could determine the strength and direction of selection during domestication (i.e., selection on wild chickens or indigenous chickens) or improvement (i.e., selection on indigenous chickens or commercial chickens). This determination is made by examining the odds ratio (OR), which is defined as the ratio of the odds of being ROH occurring in one evolutionary stage to the odds of being ROH occurring in the other evolutionary stage, in the logistic model. On the other hand, the utilization of ordinal coding {0, 1, 2} tests the trend of progressive selection for the focal window across the three continuous stages.

Gene enrichment and functional analysis

Gene enrichment analysis was performed using the Metascape (Zhou et al., 2019). Metascape identifies statistically enriched pathways and calculates the pairwise similarity between enriched pathways by Kappa statistics (Cohen, 1960). It also performs hierarchical clustering based on the pathway similarity matrix, generating a network with a threshold of the Kappa score of at least 0.3. Each pathway in the enrichment network is represented as a node and the connections between nodes indicate the correlation between the enriched pathways. We also quantified the GO-based similarity on Molecular Function (MF) between gene clusters using the mclusterSim function in the GOSemSim (Yu et al., 2010) R package. Human homologous data (org.Gg.eg.db) were used due to insufficient data in the chicken GO library.

To ascertain the risk allele of candidate genes, we queried the GWAS Catalog (Sollis et al., 2023) (www.ebi.ac.uk/gwas). In addition, we used the Gene ORGANizer (Gokhman et al., 2017) to link candidate genes and the organ system they affect. Furthermore, we extracted the functional association network for the *TRH* gene using the GENEMANIA (Warde-Farley et al., 2010) database (http://genemania.org/).

Procrustes analysis

Procrustes analysis (Peres-Neto and Jackson, 2001; Wang et al., 2010; Zhao et al., 2019; Johnson et al., 2019) assesses between-matrices similarity by minimizing the sum of squared Euclidean distances (M^2) between matrices based on linear transformations. To uncover the pattern of genetic differentiation among seven indigenous chicken breeds, we compared regional differentiation with the whole-genome background, using the Procrustes function in the VEGAN-v2.6-4 R package. The whole-genome differentiation was represented by a single seven-by-seven F_{ST} matrix calculated by the VCFtools, serving as the reference matrix in the Procrustes analysis. Regional differentiation was computed for each 200-kb genome window, resulting in 4,634 seven-by-seven F_{ST} matrices.

The *Z*-transformation of M^2 statistics for each window was produced and subsequently converted into *P*-value using cumulative probability, as described above. To identify significant windows of differentiation, the breed with the most substantial influence was further inferred using vector residuals (VR) within that specific window.

Phylogenetic distance and weighting

We constructed the NJ tree from the regional F_{ST} distance matrix calculated in the previous step. The weighted Robinson-Foulds distance (wRFD), which was implemented in the treedist function in the phangorn (Schliep, 2011) R package, was used to quantify the topological difference between NJ trees along the successive genome windows. The wRFD value ranges from 0 (identical trees) to 1 (maximum dissimilarity) with a lower value indicating greater similarity between the trees in terms of both topology and branch lengths.

Using RJF as an outgroup, we also constructed the NJ trees for the 7 indigenous chicken breeds for each 50-SNP window across the genome using the PhyML-v3.0 (Guindon et al., 2010). The frequency of occurrence (weights) for each subtree topology describing the relationship among the chicken breeds was subsequently estimated using the Twisst (Martin and Van Belleghem, 2017) software.

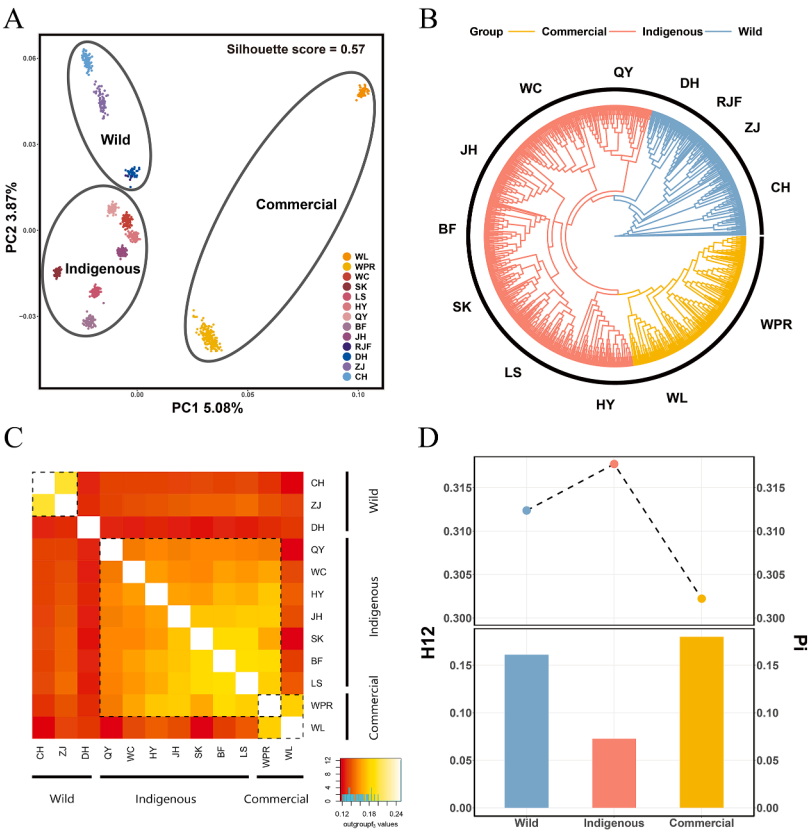

Fig. 1. Population genetic structure and diversities for chickens. (a) PCA projection of all chicken samples. (b) Unrooted neighbor-joining tree constructed by IBS distances. (c) Heatmap of pairwise outgroup-f_3 statistics of all chicken breeds, with yellow color indicating higher genetic similarity between breeds. (d) Nucleotide genetic diversity (Pi) (lines) and haplotype H12 statistic (bars) for chickens at three evolutionary stages.

Results

Wild, indigenous, and commercial chickens to be genetically distinctive

To visualize the global relationship of chickens, we performed PCA projection on genomic data from all 1,028 samples of 13 breeds (Figs. 1A and S4). We observed that the first principal component (PC1) effectively separated commercial chickens from the rest, while the PC2 divided wild chickens from indigenous ones. This distinction was supported by a reasonably high Silhouette score of 0.57 for the classification

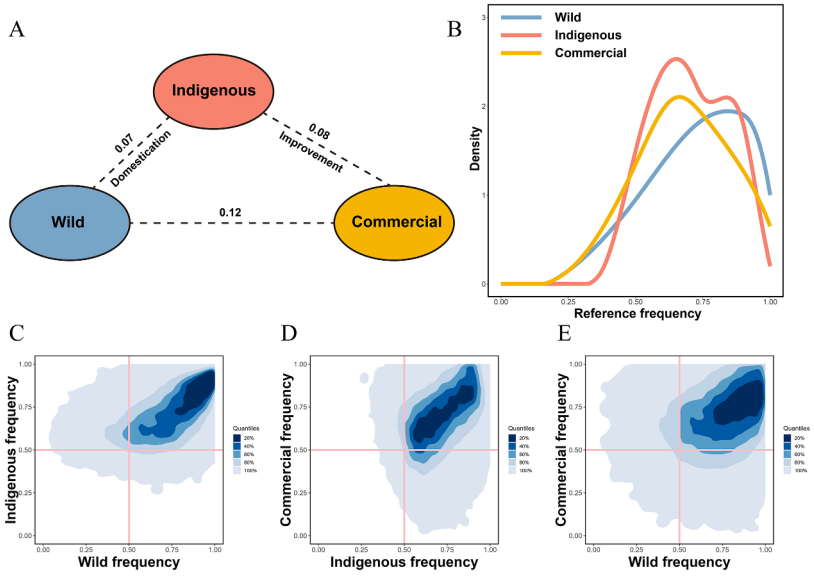

Fig. 2. Genetic differentiation and allelic change in wild, indigenous and commercial chickens. (a) Genome-wide F_{ST} between wild chickens (green), indigenous chickens (purple) and commercial chickens (yellow). (b) Allele frequency distribution of the reference alleles in wild chickens (green), indigenous chickens (purple) and commercial chickens (yellow). (c) Changes in allele frequency between wild chickens and indigenous chickens. (d) Changes in allele frequency between indigenous chickens and commercial chickens. (e) Changes in allele frequency between wild chickens and commercial chickens.

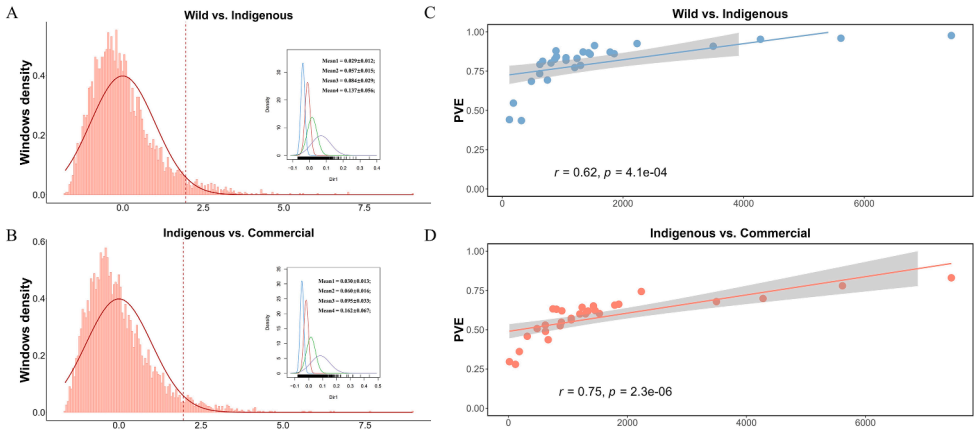

Fig. 3. Polygenic architecture of genetic differentiation during domestication and improvement. (a) The GMM partitioning of F_{ST} distributions in chicken domestication. The red line indicates the expected normal distribution. GMM partitioning suggests that F_{ST} values can be best partitioned into four distributions (the optimal number of Gaussian components is four), each characterized by specific mean, standard deviation (SD), and weight (weight 1: 0.205; weight 2: 0.334; weight 3: 0.374; and weight 4: 0.087). (b) The GMM partitioning of F_{ST} distributions in chicken improvement. Four partitioned distributions are also observed (weight 1: 0.190; weight 2: 0.304; weight 3: 0.402; and weight 4: 0.103). (c) The percentage of variance explained (PVE) by each chromosome during domestication was scaled with its size, as measured by the Pearson correlation coefficient. (d) The PVE by each chromosome during improvement was scaled with its size, as measured by the Pearson correlation coefficient.

of the three stages. In contrast to PCs that maximize the variance of the projected data, IBS distances sum the cumulative differences between samples over the genome. By transforming IBS distance matrix into individual-level NJ trees, we observed that wild, indigenous and commercial chickens formed three distinct clusters (Fig. 1B). Finally, we calculated the outgroup-f_3 statistic, which measures the degree of similarity between populations based on allele frequency differences, for breed pairs using RJFs as the outgroup. The genetic similarities within each of the three stages were higher than that between stages (Fig. 1C), confirming the results from the PCA and IBS analyses.

Based on the classification of the three stages, we calculated the corresponding genomic diversity levels. As illustrated in Fig. 1D, nucleotide genetic diversity (Pi) exhibited variation, with values of 0.312 for wild chickens, 0.318 for indigenous chickens, and 0.302 for commercial chickens. Likewise, the haplotype H12 statistic displayed variability, with values of 0.161 for wild chickens, 0.073 for indigenous chickens, and 0.178 for commercial chickens. In both measurements, indigenous chickens demonstrated the highest genetic diversity (Björnerfeldt et al., 2006; Liang et al., 2022), while commercial chickens exhibited the lowest diversity levels. Considering pooling all indigenous breeds together might lead to an inflated diversity estimation. We recalculated nucleotide and haplotype diversity statistics for individual breeds and found that the indigenous chickens still showed the highest diversity on average.

Genetic differentiations reflect polygenic architecture and genetic shifts from domestication to improvement

Domesticated animals often retain some level of genetic resemblance to their wild ancestors, and possible interbreeding of domesticated animals with their wild counterparts results in further decreased genetic differentiation (Larson et al., 2014; Larson and Fuller, 2014; Cai et al., 2022). Consistent with the expectation, the genome-wide F_{ST} between wild chickens and indigenous chickens was found to be 0.07. Surprisingly, despite specialized commercial breeding, the genome-wide F_{ST} between indigenous chickens and commercial chickens for improvement was only 0.08, a level comparable to that observed for domestication. Intriguingly, the F_{ST} between wild chickens and commercial chickens increased to 0.12, an indication of cumulative differentiation during domestication and improvement (Fig. 2A).

To explore the underlying reason for the accumulated genetic differentiation, we scrutinized the allele frequencies of chickens across the three stages. We found that in wild and commercial chickens, the allele frequencies exhibited a heavy-tailed distribution, characterized by more extreme values, both low and high. In contrast, the allele frequency of indigenous chickens constituted a taller-looking distribution with smaller dispersions (Fig. 2B). As depicted in Fig. 2C and D, most loci show minimal changes in allele frequencies during domestication and improvement, falling within the first and third quadrants. Specifically, 13.3% of loci experienced increases in frequency from wild chicken to indigenous chickens (the second quadrant), which was 2.6 times higher than the loci with decreases in frequency (5.1%, the fourth quadrant) (Fig. 2C). Conversely, 15.5% of loci witnessed a decrease in frequency from indigenous chicken to commercial chickens (the fourth quadrant), which was 2.6 times more frequent than the loci with increases in frequency (5.7%, the second quadrant) (Fig. 2D). When comparing wild chickens with commercial chickens, we observed that, eventually, 12.0% of loci experienced increases in frequency, while 13.6% of loci exhibited decreases in frequency (Fig. 2E). In other words, a substantial number of low-frequency loci in wild chickens were shifted to high-frequency loci in commercial chickens, while a comparable number of high-frequency loci in wild chickens were turned down to low-frequency loci in commercial chickens. Considering these findings collectively, it suggested allelic flipping in an 'AA-AB-BB' manner from wild chickens to indigenous chickens and then to commercial chickens took place. This phenomenon helps explain the accumulated differentiation from wild to indigenous commercial chickens and the elevated genetic diversity in indigenous chickens. Consistent with this hypothesis, the flipping was more pronounced for loci with extremely high or low frequencies in wild chickens. When considering loci within the top 10% of low or high frequencies in wild chickens, the F_{ST} between wild chickens and commercial chickens increases to 0.22. We also supplemented the Tajima's D analysis for wild, indigenous, and commercial chicken populations (Fig. S5). The results showed that Tajima's D values for all three groups were greater than zero, so a coexistence of balancing selection cannot be excluded.

As depicted in Fig. 3A and B, the distribution of F_{ST} was right skewed, with only a few loci exhibiting higher divergence while the majority displayed lower divergences. Given these characteristics, we hypothesized that the genome wide F_{ST} distribution comprised a mixture of several distributions with varying levels of divergences. Through the GMM partitioning (Fig. 3A and B), the F_{ST} values for both domestication and improvement can be best partitioned into four distributions, each characterized by specific mean and variance. These distributions

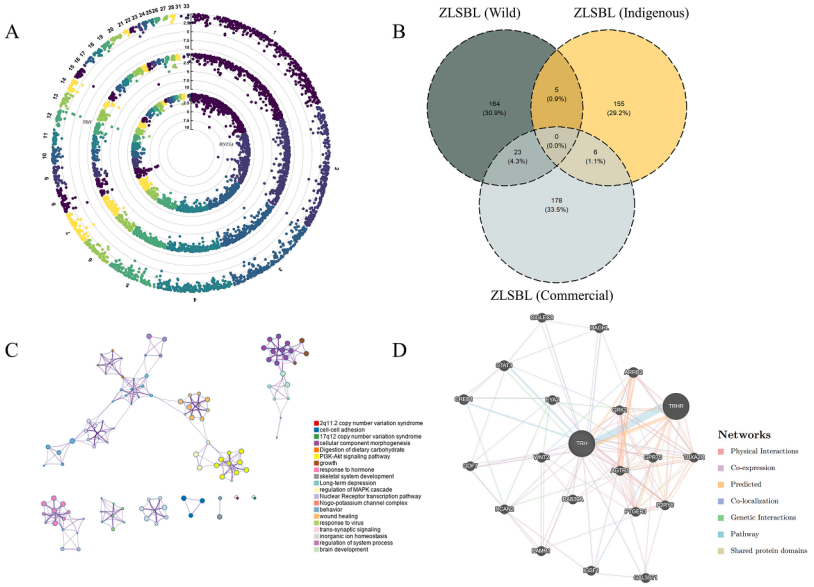

Fig. 4. LSBL analysis and functional annotation for genes under population-specific differentiation. (a) Genome-wide distribution of LSBL statistics. From the inner ring to the outer ring: wild, indigenous, and commercial chickens. (b) Overlapping of significant windows across the three stages. (c) Enrichment network constructed by similarities of enriched terms. Network nodes represent the enriched pathways. The size of the circles indicates significance. The line indicates similarity within and between clusters. (d) *TRH* gene association network.

corresponded to four classes of SNPs with different degrees of differentiations in the genome. Building upon these findings, we sought to scrutinize the genetic architecture of differentiation during domestication and improvement. We fitted all four classes of SNPs simultaneously using mixed linear models (Materials and Methods) and estimated the PVE. Notably, for both domestication and improvement, we observed that the percentage of PVE by each chromosome was positively corrected with its size (r = 0.62, P = 4.1e-04 for domestication; r = 0.75, P = 2.3e-06 for improvement). This observation suggests polygenic architecture during domestication and improvement.

In summary, the genetic differentiation observed during domestication and improvement appeared to be limited, whereas a good number of loci displayed the pattern of 'AA-AB-BB' allelic flipping. The genetic differentiation during domestication and improvement can be explained by polygenic architecture.

Distinctive population-specific differentiation in wild, indigenous and commercial chickens

Although F_{ST} statistic is commonly used to assess population differentiation, it does not offer information about the directionality of such differentiation. By evaluating the fraction of F_{ST} differentiations in a three-population tree, the LSBL method would suggest the population-specific differentiation. The reference genome was divided into 4,634 non-overlapped windows of 200-kb each to calculate window-based LSBL statistics specific to wild, indigenous and commercial chickens. We detected 193 and 103 windows in wild chickens, 166 and 79 windows in indigenous chickens, and 207 and 111 windows in commercial chickens to be significant ($P < 0.05$) and highly significant ($P < 0.01$), respectively (Fig. 4A, table S1). Not only did the indigenous chickens have the fewest candidate windows, but their mean LSBL values were also the lowest. We observed limited overlaps for significant LSBL windows between the wild, indigenous and commercial chickens (Fig. 4B).

Based on all significant LSBL windows ($P < 0.05$), we identified 493, 527, and 570 candidate genes in wild, indigenous, and commercial chickens. For wild chickens, the enriched functions were primarily associated with immune response, neurodevelopment (brain), and regulation of response to external stimuli (table S2). For indigenous chickens, the candidate genes were mainly linked to disease, metabolism (various synthetic processes), and neurodegeneration (Table S3). For commercial chickens, the candidate genes were enriched for the digestive system, sensory perception (adaptation to low-light environments), and neurodevelopment (adaptation to prolonged depression) (Table S4). Among them, the *TRH* gene (Li et al., 2020) (thyrotropin-releasing hormone), associated with growth and feeding behavior, was identified on GGA12 in both indigenous and commercial chickens (Fig. 4D). The *IGF1* gene (insulin-like growth factor 1) with known roles in controlling body size in dogs and chickens (Sutter et al., 2007; Wang et al., 2017; Qanbari et al., 2019) was identified in commercial chickens. This gene has also been associated with nervous system regulation and cell migration. Additionally, we identified several neural spine genes and signaling pathways, including the *FGF* gene family (in wild and commercial chickens) and *WNT3A* (in wild chickens), as well as both classical and non-classical *WNT* signaling pathways.

Although different sets of genes were identified by the LSBL method across chicken domestication and improvement, we proceeded to evaluate whether there exists functional similarity among these genes using GOSemSim. The result indicated that the overall functional similarity of the selected genes was not statistically significant ($P > 0.05$). Overall, our results suggest that chickens underwent distinctive differentiation processes according to the varying survival environments at different stages.

ROH-based detection of selection signatures in three stages

Population differentiation is often viewed as a result of selection. In some studies, the LSBL method was used as a proxy for the presence of directional selection. However, LSBL is not primarily designed for detecting selection, due to its certain limitations. First, like the F_{ST} method, LSBL employs an outlier approach, which does not inherently address statistical significance. Second, given that it does not necessarily leverage individual genotyping data, the accuracy is compromised due to suboptimal utilization of existing data. Third, specific topologies in some cases may result in false positives (see Fig. S6). To address these issues, we constructed generalized linear mixed effect models to identify selection signatures based on ROH. This approach not only enhances robust utilization of individual-level haplotype information but also

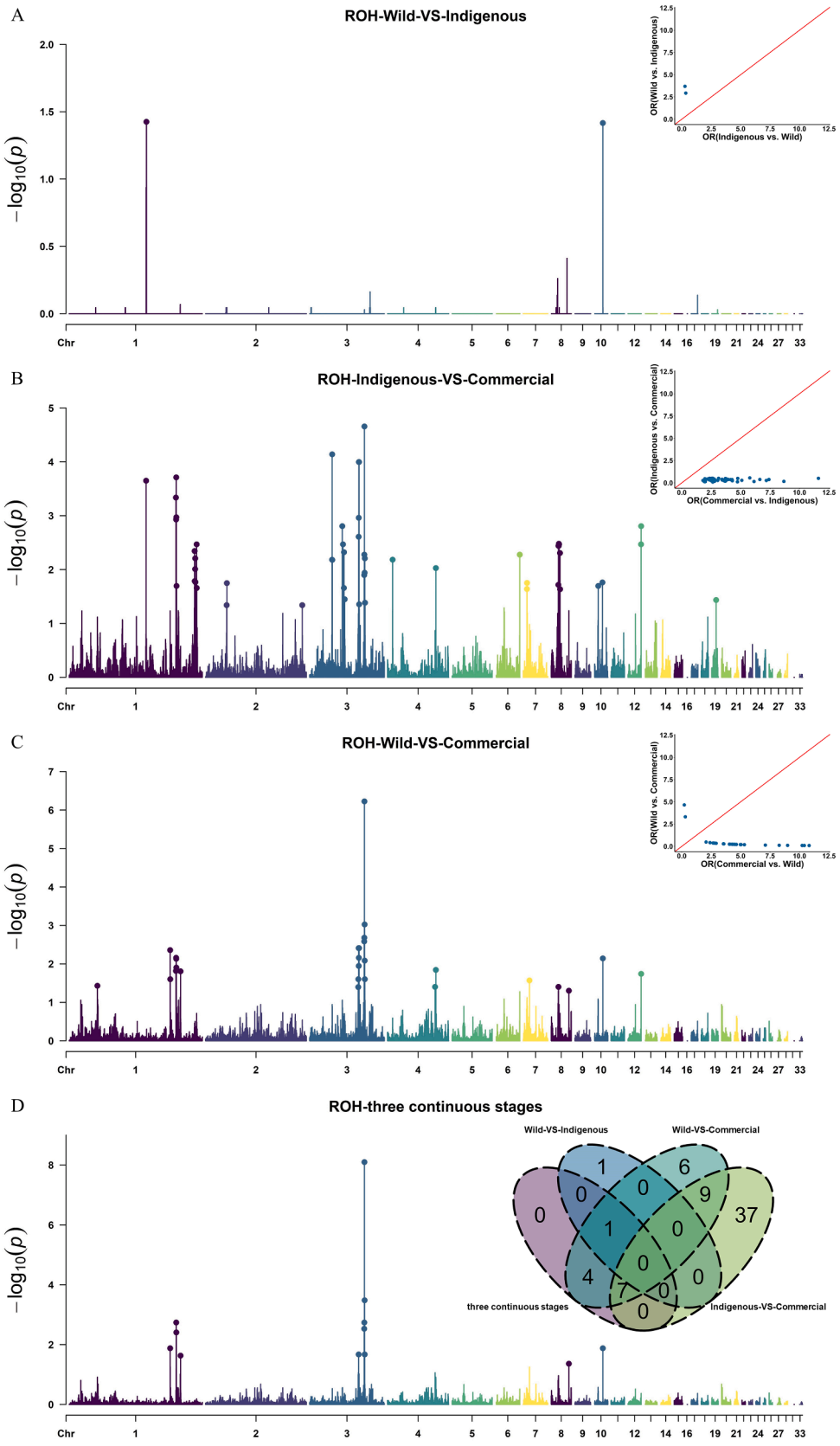

Fig. 5. The results of ROH modeling. (a)-(c) Manhattan plots of the ROH modeling signals for the comparisons between the three stages. Categorical coding is applied for the evolutionary stages. The upper right corner is the OR estimates. An OR greater than 1 signifies a higher likelihood of being ROH, indicating directional selection at the stage used in the numerator in OR calculation. (d) Manhattan plot of the ROH modeling signals for three continuous stages. Ordinal coding is applied for the evolutionary stages. In the upper right corner, the Wayne diagram displays overlapping results between the two coding strategies.

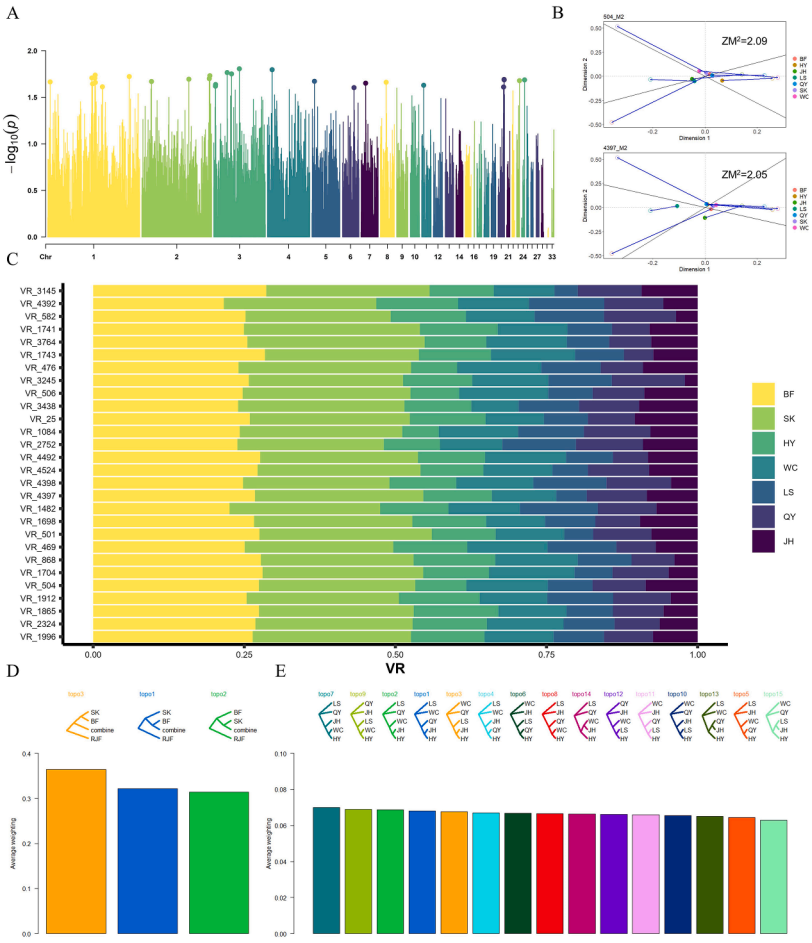

Fig. 6. Differentiation across indigenous chicken breeds. (a) Manhattan plot of genomic differentiation compared to genome background from Procrustes analysis. (b) Detailed Procrustes projections of two consecutive significant windows. Each set of local F_{ST} matrix and global F_{ST} matrix is connected by a solid blue line, the hollow and solid dots correspond to two sets of F_{ST} matrices, and the colors of the dots represents the subspecies of indigenous chicken breeds, where the lines indicate the VR. (c) Stacked distributions of residual vectors for windows exhibiting high heterogeneity in indigenous chicken breeds (Beijing Fatty Chicken (BF), HuiYang Bearded chicken (HY), Jinhu chicken (JH), LangShan chicken (LS), QingYuan chicken (QY), Silkie chicken (SK), and WenChang chicken (WC)). (d) Phylogenetic weighting in the Twisst analysis of four taxa. Indigenous chicken breeds except SK and BF are combined into a single taxon. RJFs are used as the outgroup. (e) Phylogenetic weighting in the Twisst analysis of five taxa. SK, BF, and RJFs are removed. Unrooted phylogenetic tree is used.

demonstrates improved interpretability by clearly defining statistical significance.

In comparison to the LSBL design, we first modeled the evolutionary stages as categorical variables to detect selections in wild, indigenous or commercial chickens (Materials and methods). Two significant windows were detected in the comparison between wild chickens and indigenous chickens (GGA1: 114600001-114800000; GGA10: 13200001-13400000). By examining the OR, we found that in both windows, the odds of ROH were higher in wild chickens than in indigenous chickens (OR (wild vs. indigenous) $>$ 1, as illustrated in Fig. 5A). No surprise, we also observed a higher genetic diversity in indigenous chickens compared to wild chickens in both windows. Within these windows, we identified 21 candidate genes, including *PLIN1* on GGA10, associated with regulating the response to cold temperature stimuli, *KIF7* linked to congenital malformations, *POLG* associated with neurological and ocular diseases as well as inborn metabolic disorders, and *FANCI* involved in the regulation of the cardiovascular and hematological system, along with other related diseases. A total of 53 significant windows were identified in the comparison between indigenous and commercial chickens (Fig. 5B), with the most prominent windows located on GGA3. The OR consistently favored ROH occurring in commercial chickens (OR (commercial vs. indigenous) $>$ 1). These windows covered 193 candidate genes, among which were noteworthy genes such as protein kinase *PRKD3* implicated in sphingolipid biosynthesis, *VIP* associated with psychiatric disorders, *KCNQ5* linked to mental and behavioral disorders, and *RIMS1* related to neurological disorders and eye diseases. Using Gene ORGANizer, these genes were categorized into several groups including digestive system functions (involving carbohydrate and starch metabolism and salivary secretion, for genes such as *AMY1A, AMY1B, AMY1C, AMY2A*, and *AMY2B* from the *AMY* gene family), light-stimulated sensory perception (*OLFM3*), eating behavior (*TRH*), positive regulation of nervous system development (*GRM5*), and response to temperature stimuli (involving *TPR, TRPV2*, and *TRPM8*). Lastly, a total of 27 significant windows, covering 78 candidate genes, were identified in the comparison between wild chickens and commercial chickens. The examination of the OR (Fig. 5C) revealed two windows with a preference for ROH in wild chickens (OR (wild vs. commercial) $>$ 1), and notably, one window overlapped with the significant window detected in the comparison between wild and indigenous chickens. In contrast, the remaining 25 windows favored ROH in commercial chickens (OR (commercial vs. wild) $>$ 1). Particularly, we did not observe any windows where the odds of ROH were higher in indigenous chickens relative to wild chickens and commercial chickens. While only a limited number of significant windows identified by the ROH method overlapped with significant LSBL windows, these overlapping windows consistently demonstrated high significance in the

LSBL results ($P < 0.01$, Fig. S7).

The ROH modeling approach provides a unique advantage for testing consistent selections within specific genomic regions from the wild chickens compared with commercial chickens. In this case, we utilized ordinal coding for the three continuous states, assigning 0 for wild chickens, 1 for indigenous chickens, and 2 for commercial chickens in the model. The results unveiled 12 significant windows covering 42 candidate genes, all of which were identified as significant ($P < 0.05$) in earlier steps (Fig. 5D). Upon examining the model coefficients, we identified two genomic regions of GGA1: 165200001-165400000 and GGA10: 13200001-13400000, undergoing selection relaxation from wild chickens to commercial chickens (negative coefficient or the odds of ROH were higher in wild chickens than in commercial chickens). Alongside previously detected candidate genes *PLIN1, KIF7*, and *POLG*, we discovered a few new genes such as *TICRR, PEX11A*, and *RHCG* within these regions. Conversely, the other 10 windows exhibited consistent selection from wild chickens to commercial chickens (positive coefficient or the odds of ROH were lower in wild chickens than in commercial chickens). These windows were primarily located on GGA3 with one exception on GGA8 (GGA8: 26400001-26600000). We found that the human homologues of candidate genes identified in the ROH analysis all appeared in the GWAS catalog database. This suggests functional similarity in chicken phenotypic alterations and human diseases. Notably, among these genes, *POLG* and *TRH* were annotated with a wide range of traits and diseases in association studies.

Non-selective differentiation across indigenous chicken breeds

While selection is a potent force driving population differentiation, non-selective processes such as genetic drift and geographic isolation, also play significant roles in shaping differentiation between populations. Despite not experiencing a strong selection, PCA projections (Fig. 1A) still indicated distinctive differentiation among indigenous chicken breeds. To validate such differentiation was more likely influenced by genetic drift, we calculated the ratio of the genomic inflation factor to the largest eigenvalue using EigenGWAS. By contrasting this ratio from all 13 breeds to that from seven breeds of indigenous chickens, we observed a higher value for indigenous chickens (40.3/36.8=0.913) compared to that from all chickens (63.0/71.3=0.884) (Fig. S8). This suggests the differentiation of indigenous chicken breeds is strongly influenced by genetic drift.

To further analyze the pattern of differentiation across indigenous chicken breeds, we conducted a Procrustes analysis by comparing each of the 4,634 genomic windows to the whole-genome background and identified 28 windows exhibiting significant large differentiation ($P < 0.05$) (Fig. 6A). To assess whether these 28 windows tended to cluster in the genome, we performed the runs test (Zhang et al., 2019b) that rejected a random distribution of these significant windows across the genome ($P < 0.05$). Three regions showed the enrichment of differentiation, namely GGA1:101200001-102400000 (504_M^2), GGA3:3600001-4200000 (1741_M^2), and GGA20:12000001-13400000 (4397_M^2). A total of 73 genes were identified within the 28 significant windows, including genes associated with the negative regulation of neurogenesis (e.g., *PAX6* and *DIXDC1*), genes influencing neuronal migration (*PAX6* and *PEX7*), genes involved in starch and sucrose metabolism (*PYGB* and *AGL*), and a gene responsible for cellular responses to external stimuli (*MAP3K5*). This suggests that indigenous chickens may vary in related physiological functions. To determine whether these regions were hotspots of genetic differentiation across all breeds or specific to a particular breed, we examined the VR of each significant window and observed significantly higher percentages of VR values in the 28 windows of BF and SK compared to the other breeds (Fig. 6C). As we compared each window to the whole-genome background, the Procrustes analysis could not specify the direction of differentiation. We therefore assessed the differences between successive windows using wRFD based on the phylogenetic tree topology constructed for each window. The genome average of wRFD values (Fig. S9) was 0.523, indicating a substantial differentiation (unordered fluctuations) between successive windows.

To further validate our findings, we employed Twisst to iteratively sample subtrees and assign weights to the topologies of trees representing indigenous chicken breeds. Building on the Procrustes analysis result, we initially constructed three topology-weighted subtrees for four taxa (SK, BF, all other indigenous chicken breeds, and RJF. Here all other indigenous chickens including LS, QY, JH, WC, and HY), of which BF and SK exhibited the highest proportion (0.36) of topology weights at the distal position of the tree (Fig. 6D). Subsequently, we constructed subtrees consisting of 15 topologies for five taxa by excluding SK and BF. In this case, the weight of each topological structure was relatively uniform (about 7%) and there was no dominant topology (Fig. 6E). The Twisst results supported the conclusions drawn from the Procrustes and wRFD analyses. The level of variation in most breeds appeared to be comparable, aligning with the neutral expectation of differentiation in indigenous chicken breeds. The differentiation observed in these breeds was likely attributed to the accumulation of random variation and drift across breeds, counteracting potential effects caused by genetic exchange between them (Lopes et al., 2023). The significant differences observed in BF and SK, as compared to the other indigenous chickens, may be due to distinct ancestral origins.

Discussion

Chickens have abundant phenotypic and genotypic variations, coupled with a clear domestication history, making them an excellent model for studying in evolutionary genetics (Diamond, 2002; Wang et al., 2020). In this work, we conducted a comprehensive analysis of genomic changes in chickens throughout domestication and improvement. In contrast to previous studies that solely focused on comparing genomic changes for two stages, our investigation spans the entire process from wild to indigenous chickens up to commercial chickens. By placing indigenous chickens at the center of our analyses, we gain valuable insights into the genetic basis and processes of chicken domestication and improvement. The evolutionary patterns uncovered in chickens also contribute to our understanding of domestication in other animals.

We recognize that the relatively limited marker density of the microarray data may raise concerns about the ability to detect selective traits across breeds. However, it is important to note that the linkage disequilibrium (Fig. S2) between markers on the Illumina 60 K chip (Groenen et al., 2011) is sufficiently strong that genetic patterns and trends can be accurately inferred without significant loss of information (Sallam and Martsch, 2015; Alqudah et al., 2020). Although the marker density is not as high as the resequencing data, this density is sufficient to capture large-scale genetic trends and provide insights into the genetic structure of the population under study (Malomane et al., 2018).

We observed elevated levels of genetic diversity in indigenous chickens compared to both wild and commercial chickens. In modern chicken breeding, local chicken breeds are often used to improve the traits of commercial chickens through crossbreeding. The indigenous chickens act as a reservoir for genetic diversity (Malomane et al., 2019). Similar higher diversity in domesticated animals compared to their wild counterparts have been documented in other species such as tiger, honeybees and pigs, as well as in crops like rice (Frantz et al., 2015; Lin et al., 2023; Gu et al., 2023; Gao et al., 2023; Lan et al., 2024). Our analysis of allelic changes and genomic selection signatures in indigenous chickens suggests that their increased genetic diversity may be attributed to the lack of intense purifying selection. Indigenous chickens have been protected by humans, which reduces the selective pressures they face (Desta, 2021; Desta and Wakeyo, 2024). This reduced pressure likely facilitates the observed pattern of 'AA-AB-BB' allelic flipping, contributing to their heightened genetic diversity. Base on the concept of adaptation building on what has already presented, the presence of

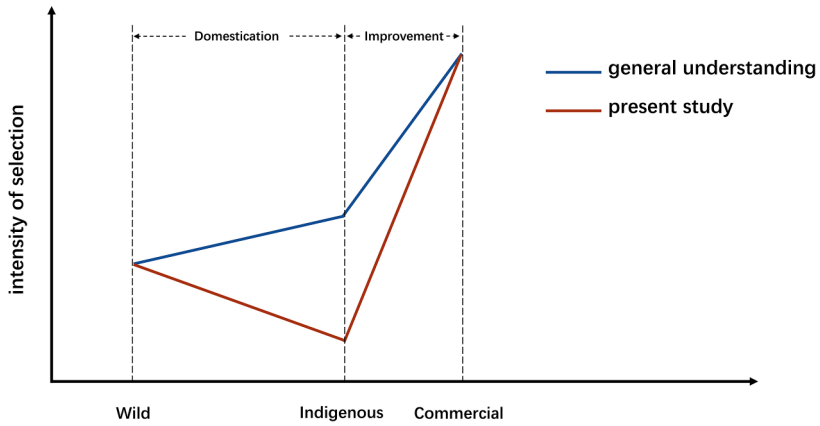

Fig. 7. An illustration of selection intensity trends among wild, indigenous, and commercial chickens. The blue line represents the general understanding based on previous reports, while the red line represents the findings from the present study. The x-axis categorizes the evolutionary stages into wild, indigenous, and commercial, and the y-axis is the intensity of selection. The present study reveals a different trend compared to the general understanding, highlighting a lower intensity of selection in indigenous chickens.

standing genetic variation at medium to high frequencies can potentially facilitate rapid adaptation to new environments or artificial selections. This is consistent with the findings by Luo et al. that Chinese indigenous chickens, except those breeds having muffs and beard phenotype, were less intensively selected (Luo et al., 2020). However, we cannot completely exclude the coexistence of balancing selection (Fig. S5). According to previous studies, balancing selection is observed in multiple indigenous chicken populations, with the associated selective markers offering high polymorphism for estimating genetic diversity while concurrently reducing genetic divergence among populations (Arlud et al., 2016).

Quantitative traits are generally considered as polygenic (Yang et al., 2011b; Yengo et al., 2022) and selection for these traits is likely to act on many pre-existing genetic variants with small effects (Turchin et al., 2012). Because selections "flatten" on multiple loci simultaneously, the shift of allele frequencies at each locus is likely to be small. It is worth noting that a large number of loci implies weaker selection, as strong selection on many variants would likely lead to excessive loss of competing lineages and population collapse. Population genetic models propose a viability threshold of 50 to 100 co-selected loci (Hufford et al., 2012; Allaby et al., 2015; Alam and Purugganan, 2024). The uncovered molecular basis of domestication and improvement aligns with the genetic architecture of complex traits. We found only a few loci with significant differentiation or selection signatures, even for specialized commercial chickens. Conversely, we validated the polygenic differentiation during domestication and improvement. The pattern of polygenic differentiation suggests that both domestication and improvement are continuous evolutionary processes that unfold over time. Loci that do not meet the selection threshold could still contribute to environmental adaptation. Our findings based on LSBL analysis may be considered as an indication of distinctive polygenic adaption preferences at different stages of chicken evolution. While wild chickens were exposed to selection for immunity and responsiveness to external stimuli, indigenous chickens were subjected to pressures related to metabolism and potentially weakened neurological function. In contrast, commercial chickens experienced strong selection favoring growth and sensory perception.

Interestingly, we identified multiple genes associated with neural spine cell development, including those in the *FGF* family and *WNT* signaling pathway, known to play critical roles in neural crest development. These findings support the neural crest hypothesis of domestication or domestication syndrome (Wang et al., 2013, 2018; Naval-Sanchez et al., 2018; Alberto et al., 2018; Daly et al., 2018; Wilkins and Wrangham, 2014,), which suggests that the animal domestication is directly or indirectly caused by defects in neural crest cells during embryonic development relative to their wild ancestors (Wilkins and Wrangham, 2014). The *WNT* signaling pathway play an impact on the development of neural crest cells through studies in knockout mice (Banerjee et al., 2011). The *WNT* signaling pathway play an important role in embryonic development, particularly in the nervous system. Mutations in the *WNT* gene family result in the absence or abnormality of neural tissues such as the midbrain, hippocampus, spinal cord, and neural crest.

Frequency-based methods for detecting selection signatures often underutilize information from individuals and lack clear and flexible statistical models to quantify differences and ascertain the direction of selection. While people tend to consider the selection to occur at a higher stage of evolution, we showed that it is not necessarily the case. To enhance the detection of selection signatures of major effects, we introduced a generalized linear mixed model utilizing the ROH statistics. With the ROH model, we identified the selection signatures occurring in wild and commercial chickens, as well as the signatures persisting throughout the entire transition from wild chickens to commercial chickens. Combined with the elevated levels of genetic diversity in indigenous stage and the pattern of 'AA-AB-BB' allelic flipping, we propose that during chicken domestication and improvement, the selective pressure is not constantly increasing (Fig. 7).

In summary, our study provides a thorough investigation into genomic changes and genetic differentiation occurring during domestication and improvement. The insights gained not only deepen our understanding of chicken domestication but also provide valuable guidance for exploring patterns in the domestication of other animals.

CRediT authorship contribution statement

Zilong Wen: Conceptualization, Methodology, Software, Validation, Formal analysis, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Xinyu Cai:** Conceptualization, Methodology, Software, Validation, Formal analysis, Data curation, Writing – original draft, Visualization, Writing – review & editing. **Zexuan Liu:** Software, Writing – review & editing. **Lizhi Tan:** Software, Investigation, Data curation, Writing – review & editing. **Yuan Kong:** Software, Investigation, Writing – review & editing. **Yuzhan Wang:** Investigation, Writing – review & editing. **Yiqiang Zhao:** Conceptualization, Methodology, Resources, Writing – original draft, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no conflict of Interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psj.2025.105081.

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