

MAGIC POPULATION: ROLE IN CROP IMPROVEMENT

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INTRODUCTION:

An effective breeding program requires a genetically diverse population and an understanding of the genetic basis of that population. Most commercially important traits are controlled by quantitative trait loci (QTL), which present a challenge for plant breeders to identify. Traditional QTL mapping populations, derived from dihybrid crosses, offer only a limited view of the genetic factors affecting target traits due to a narrow genetic base, limited recombination, and lack of diversity confined to the two parents. Additionally, factors such as linkage disequilibrium (LD), population substructure, uneven allele frequencies, uncertain pedigrees, and missing parental information reduce the effectiveness of Genome-Wide Association Studies (GWAS), which were developed as an alternative to biparental populations.

Weaknesses in existing designs have led to a new class of complex experimental designs, conjunctive designs, and intermediate to bipolar mapping of power, diversity, and resolution. Multi-parent Advanced Generation InterCrosses (MAGICs) is developed by crossing multiple inbred progenitors for many generations before creating inbred lines, resulting in a diverse population whose genomes are large mosaics.



STAGES OF DEVELOPING MAGIC POPULATION

1. Founder selection

Based on genetic and/or phenotypic diversity, founder lines are selected from diverse origin (global germplasm collections, distant relatives) or material with a more restricted set of origins (e.g., elite cultivars, local adaptability). Typically, there are eight founders, though this varies depending on the goal and design of the experiment.

2. Mixing

In this phase, inbred founders are paired and interbred in a specific order to develop recombinant inbred lines (RILs) that incorporate genetic contributions from each founder. Two approaches are used for mixing:

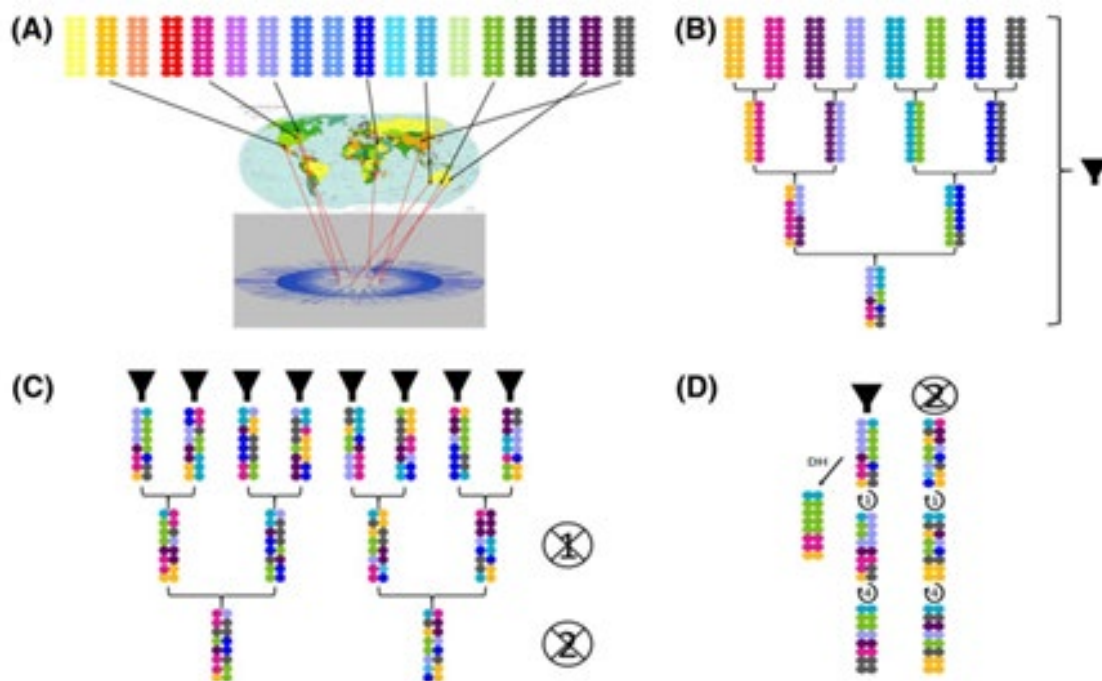
- ✓ Funnel Approach: Involves several generations of crossing elite lines, followed by intercrossing hybrids to combine all founder genomes. This method is often used for plants that are challenging to cross.
- ✓ Diallel Approach: All possible combinations of crosses between founders are made, creating a broad genetic base and a wide range of allele combinations.

3. Advanced intercrossing

Mixed lines from different funnels are randomly intercrossed to increase recombination. This enhances the population's QTL mapping capability, with at least six rounds of intercrossing recommended.

4. Inbreeding

Homozygous RILs are produced either through doubled haploid production or single-seed descent. While doubled haploid production is faster, several generations of selfing introduce additional recombination, which can be beneficial for future studies. Typically, it takes at least eight crop seasons to reach the S5 generation to develop MAGIC populations.



A) Founder lines selection. B) Mixing founder lines in funnel. C) Advanced intercrosses. D) Inbreeding by SSD or double haploidization

POPULATION SIZES

The strength and resolution of QTL mapping increase with population size. For coarse QTL mapping, a population of 50–250 individuals are often required. To achieve sub-centimorgan resolution and identify single QTLs accounting for 5% of phenotypic variability, large-genome organisms require at least 500 progenies.



APPLICATIONS OF MAGIC POPULATIONS

- 1. Permanent immortal mapping populations for precise QTL locating:** MAGIC populations are valuable genetic resources for linkage and association studies in QTL finding. The increased recombination rate enhances QTL mapping precision, reduces LD, minimizes population structure, and prevents false positives. The mixed genetic background increases the number of segregating QTLs and promotes unique allele rearrangements, enabling the targeting of multiple phenotypes.
- 2. Development of New Elite Material:** RILs developed from MAGIC populations can be immediately released or used as pre-breeding materials in breeding pipelines to create improved lines, hybrids, or new cultivars.
- 3. MAGIC populations allow for the simultaneous exploration of cytoplasmic effects, genome introgressions, and chromosomal recombination, affecting allelic diversity across the genome.** When combined with known genome sequences, they enhance the discovery of putative causal polymorphisms underlying QTLs, leveraging advancements in high-throughput genotyping and phenomics platforms in the post-genomics era.

DATA MANAGEMENT

a) Management of large genetic resource populations

Genotypic and phenotypic data from MAGIC populations should be shared across multiple research groups. Platforms like Agrobase, iPlant, and Phenome networks can manage data, design experiments, and conduct bioinformatics studies (Huang et al., 2015).

b) High-throughput genotyping

Individuals may be genotyped at different inbreeding stages, leading to varying heterozygosity and genome structure. Genotyping across platforms can cause systematic missing data. While advancing genotyping-by-sequencing technologies is expected to lower costs and increase adoption, maintaining data coherence over time remains a challenge.

c) High-throughput phenotyping

High-throughput phenotyping can occur at the molecular level, producing thousands of traits representing gene, protein, or metabolite expression, or at the individual plant level across different environments, years, and conditions. Advances in sensors, robotics, and imaging will revolutionize data collection for large field trials and controlled environment experiments, maximizing the strengths of MAGIC populations (Araus and Cairns, 2014).

GENETIC ANALYSIS

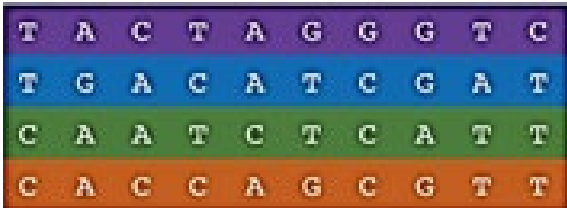
Genetic analysis of MAGIC populations, though similar to that of biparental populations, must account for the unique features of the design, such as multiple founder alleles.

a) Linkage map construction

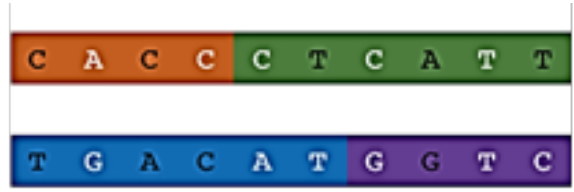
In MAGIC populations, increased recombination is most evident around centromeres, where biparental populations show minimal marker separation. Markers spaced at least 2 cM apart can be reliably ordered in four-parent MAGIC populations of 500 lines, improving to 1 cM resolution in larger populations of 1,000 lines (Cavanagh et al. 2013). As resources grow, a physical map or reference sequence will serve as a benchmark for validating genetic maps and verifying sequence assemblies.

b) Haplotype mosaic reconstruction

The reconstruction of haplotype mosaics from high-density genotyping data enables highly accurate estimation of recombination breakpoint positions. Three forms of genetic data representations emerge from the haplotype reconstruction process in MAGIC populations: mosaics, founder probabilities, and marker scores. High-density genotyping data enables accurate haplotype mosaic reconstruction, which is crucial for determining QTLs and recombination hotspots. MAGIC populations offer higher resolution than biparental RIL populations, providing more detailed insights into genomic structure.



Founder haplotypes



Inferred mosaics for RIL's

c) QTL mapping

Two main approaches for QTL mapping in MAGIC populations are the biallelic method (BA), which uses marker scores like in biparental populations, and the probabilistic parentage method (PPA), where each marker corresponds to a single parental allele. A more general approach is linkage disequilibrium and linkage analysis (LDLA) mapping, uses haplotypes, shows similar effects but doesn't require all founders to have different effects. This condition is adaptable with multiple founders.



ANALYSIS SOFTWARE FOR GENETIC GAP CONSTRUCTION AND QTL MAPPING

The higher complexity of multiparent population designs requires a flexible and general framework for analyses capable of reconstructing founders' haplotype mosaics, to impute whole-genome genetic variants, and to handle multiple founder alleles and their population structures. Therefore, different R packages started. The QTL mapping software like the R package HAPPY, an interval mapping approach method based on founder probabilities, the R/mpMap package allows mapping QTLs through simple linear regression model, R/mpMap2 and magicMap R packages have been extended to other multi-parental population, R/qlt2 package that offers possibility to use regression models based on the Haley-Knott regression method.

The most used alternative is the Trait Analysis by aSSociation, Evolution and Linkage (TASSEL) software that uses phenotypic and genotypic data. Furthermore, some R packages are also available to conduct GWAS such as the so-called Genome Association and Prediction Integrated Tool (GAPIT) A whole-genome average interval mapping (WGAIM) approach was renamed as approach to multivariate multiparent (MVMP) WGAIM for QTL analysis with multiple alleles in a multi-environment or multi-trait data.



LIMITATIONS

They need more investment in time and greater efforts to be developed due to their convoluted crossing scheme involving multiple founder lines and a large number of selfing generations. The population goals should be clearly defined before initiating population development since MAGIC populations require a larger population size compared to a bi-parent population for fine genetic mapping also, which not only hinders population development but also limits phenotypic traits to evaluate. The presence of multiple founders involved in population development makes the process logistically challenging and labor-intensive.

When wild species are in the panel of founder parents to broaden the genetic diversity, genetic and genomic incompatibility may appear. In addition, it is important to consider that the complexity of the funnel crossing schemes poses a potential intermating bias that can result in assortative mating instead of the assumed random mating that introduces a generation of genetic subgroupings and distorts LD.



CONCLUSION

The MAGIC populations are recombinant inbred sets that result from the intercrossing of multiple parents creating a vast genetic diversity. Although the development of MAGIC populations requires considerable efforts, theoretical and real studies show that MAGIC populations represent powerful tools for the detection of QTLs present in the set of parents, with considerable advantages over bi-parental and germplasm sets for the detection of QTLs. As the number of MAGIC populations is continuously growing, new tools for an efficient analysis of MAGIC populations have recently been developed. We are confident that MAGIC populations will play an important role in addressing the formidable challenges faced by breeders in a scenario of climate change and the increased demand of plant products by significantly contributing to the development of new generations of resilient, highly productive, and resource-efficient cultivars.