



this is "totally not a spoof".

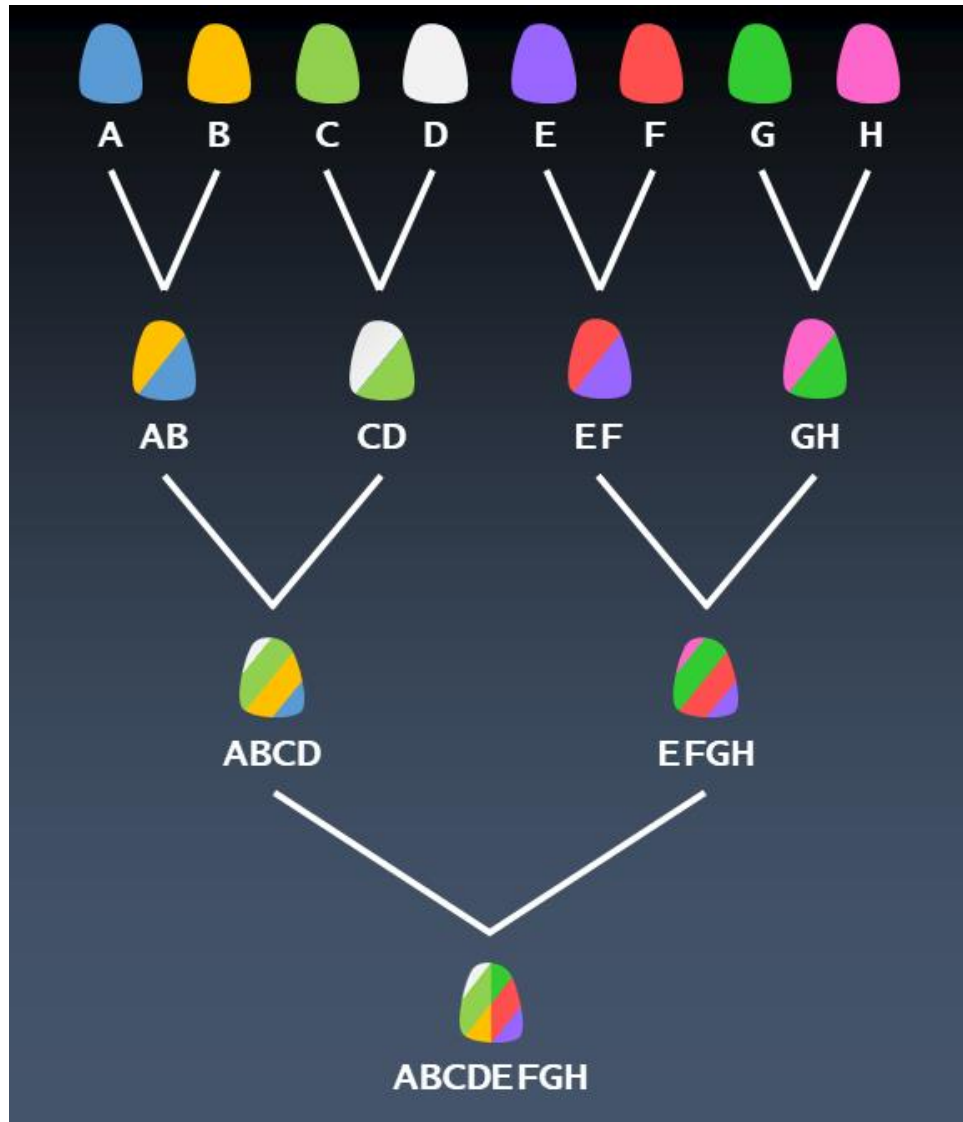
MAGIC population design

CJ Yang

Scotland's Rural College

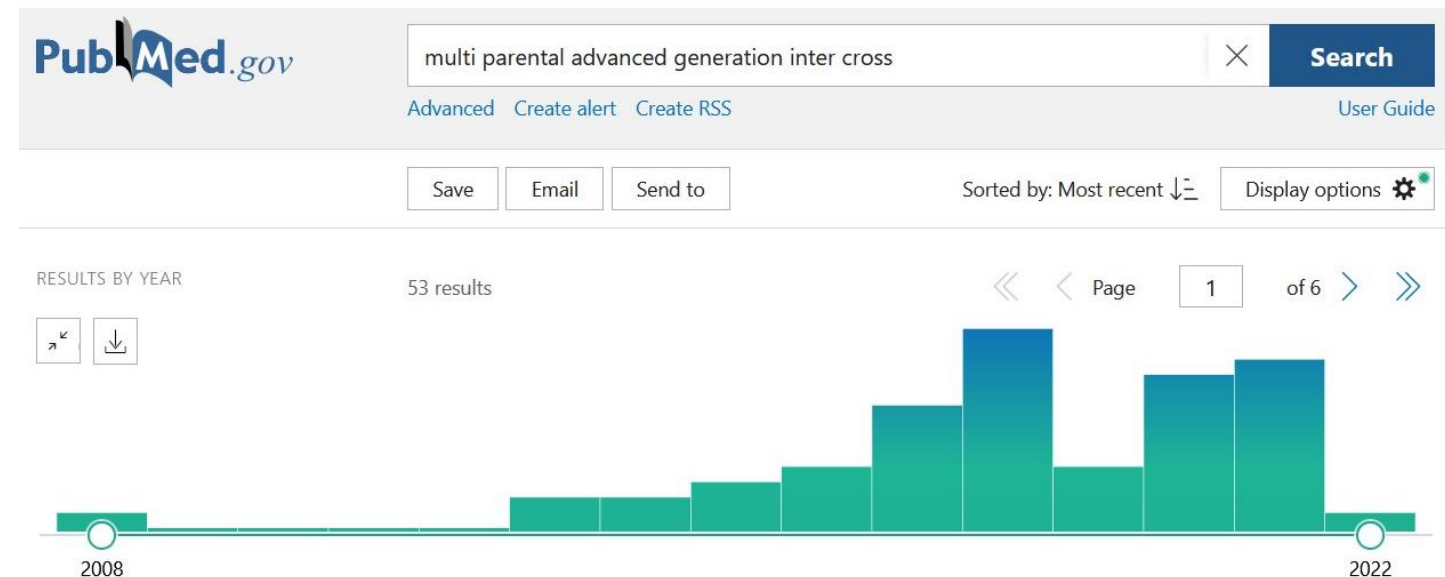
April 7th, 2022

Introduction



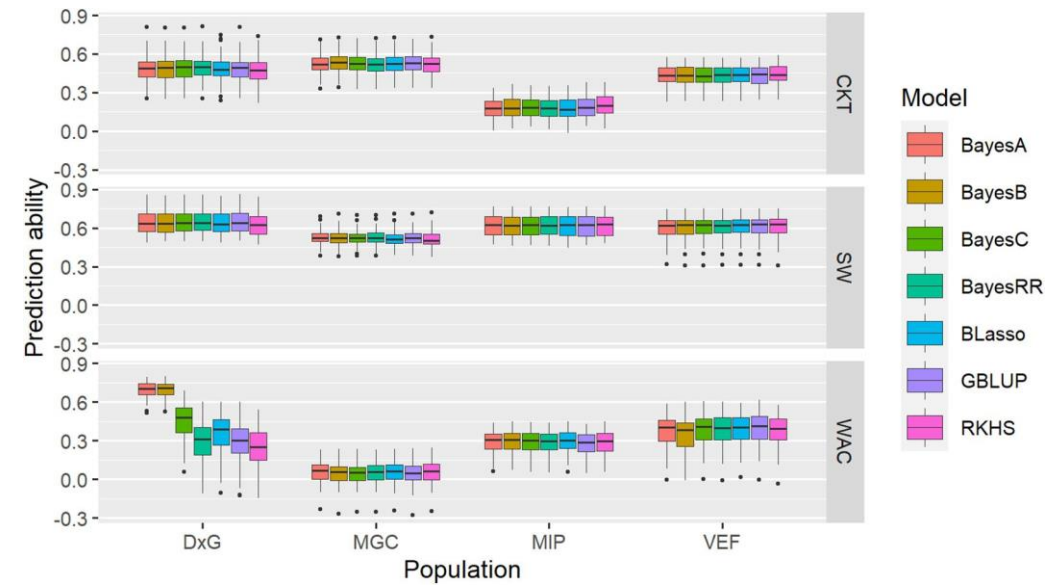
Multi-parental **A**dvanced **G**eneration **I**nter-**C**ross

- Experimental multi-parental population with a rich recombination landscape
- First described in plants by Mackay and Powell (2007)
- Derived from Heterogeneous Stock (HS) (Mott et al 2000) and Collaborative Cross (CC) (Churchill et al 2004) in mice
- First MAGIC with 19 Arabidopsis founders (Kover et al 2009)

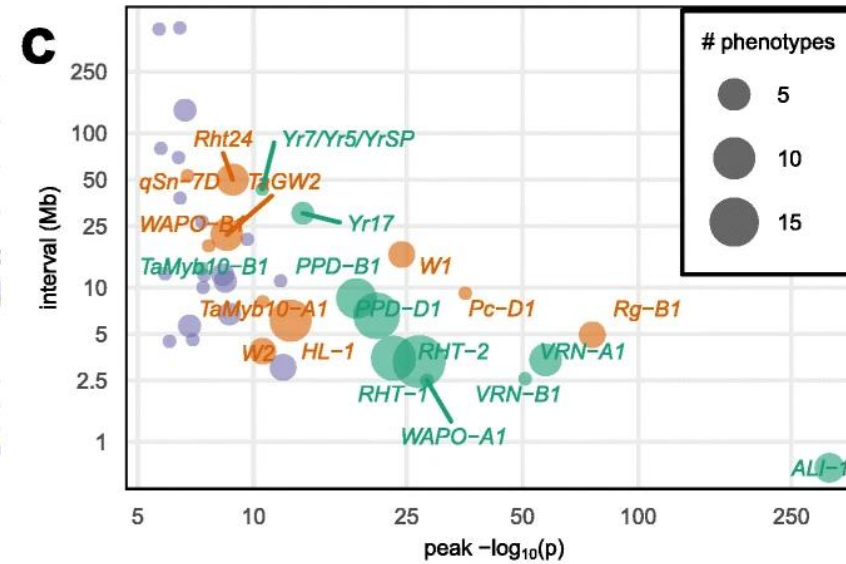
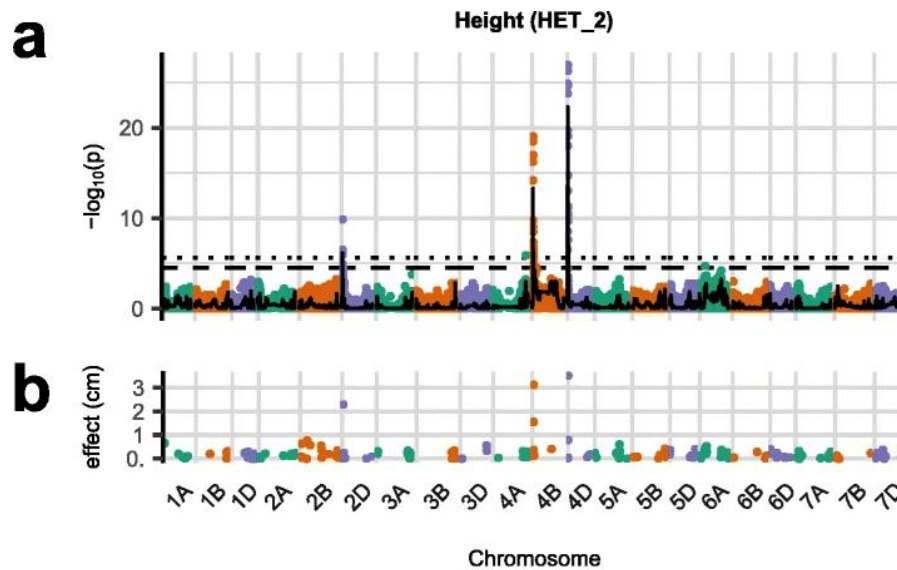


In practice

1. QTL mapping
2. Genomic prediction
3. Breeding new varieties
4. Genetic resources



Diaz et al (2021) Genetic architecture and genomic prediction of cooking time in common bean (*Phaseolus vulgaris* L.)

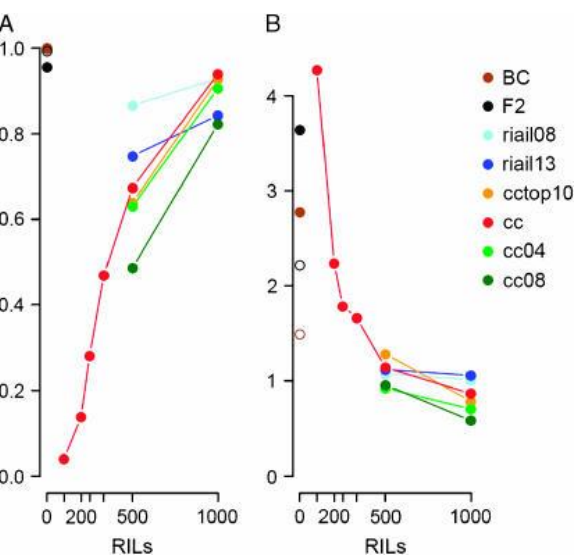


Scott et al (2021) Limited haplotype diversity underlies polygenic trait architecture across 70 years of wheat breeding

Properties

Advantages

- 1. Broad applications
- 2. Minimal population structure
- 3. High mapping power and resolution
- 4. Longevity



Valdar et al (2006) Simulating the Collaborative Cross: Power of Quantitative Trait Loci Detection and Mapping Resolution in Large Sets of Recombinant Inbred Strains of Mice

Disadvantages

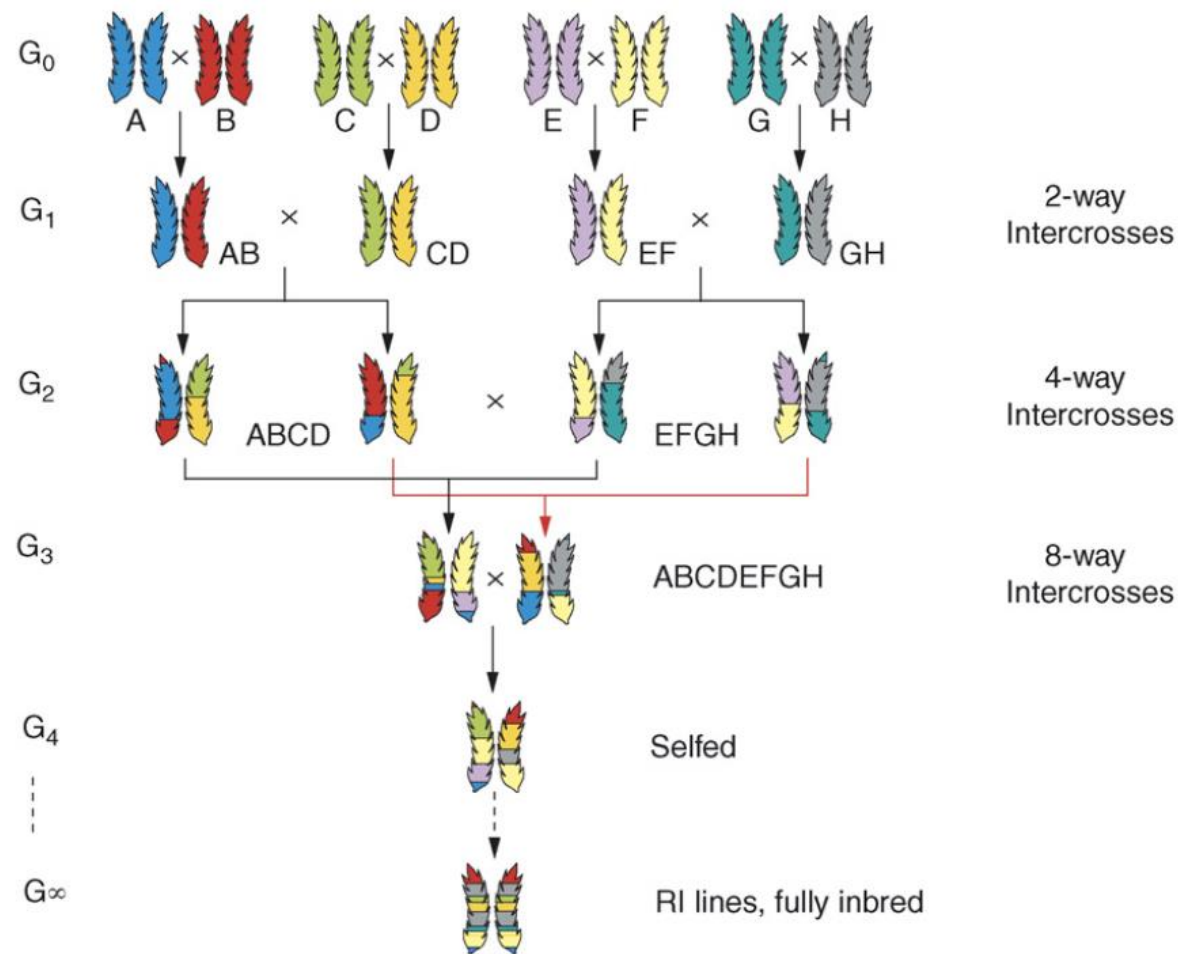
- 1. Time consuming

Table 1			
Relative strengths and weaknesses of three methods for the identification of QTL in crops, bi-parental linkage analysis (linkage), association mapping (association) and Multi-parent Advanced Generation Inter-crosses (MAGICs)			
Application	Linkage	Association	MAGIC
Suitability for coarse mapping	+	—	+
Suitability for fine mapping	—	+	+
Low genotyping requirement	+	—	—
Low phenotype requirement	+	—	—
Resistant to population substructure	+	—	+
Relevance to breeders	—	+	+
Relevance over time	—	+	+
Time to establish	—	+	—

Cavanagh et al (2008) From mutations to MAGIC: resources for gene discovery, validation and delivery in crop plants

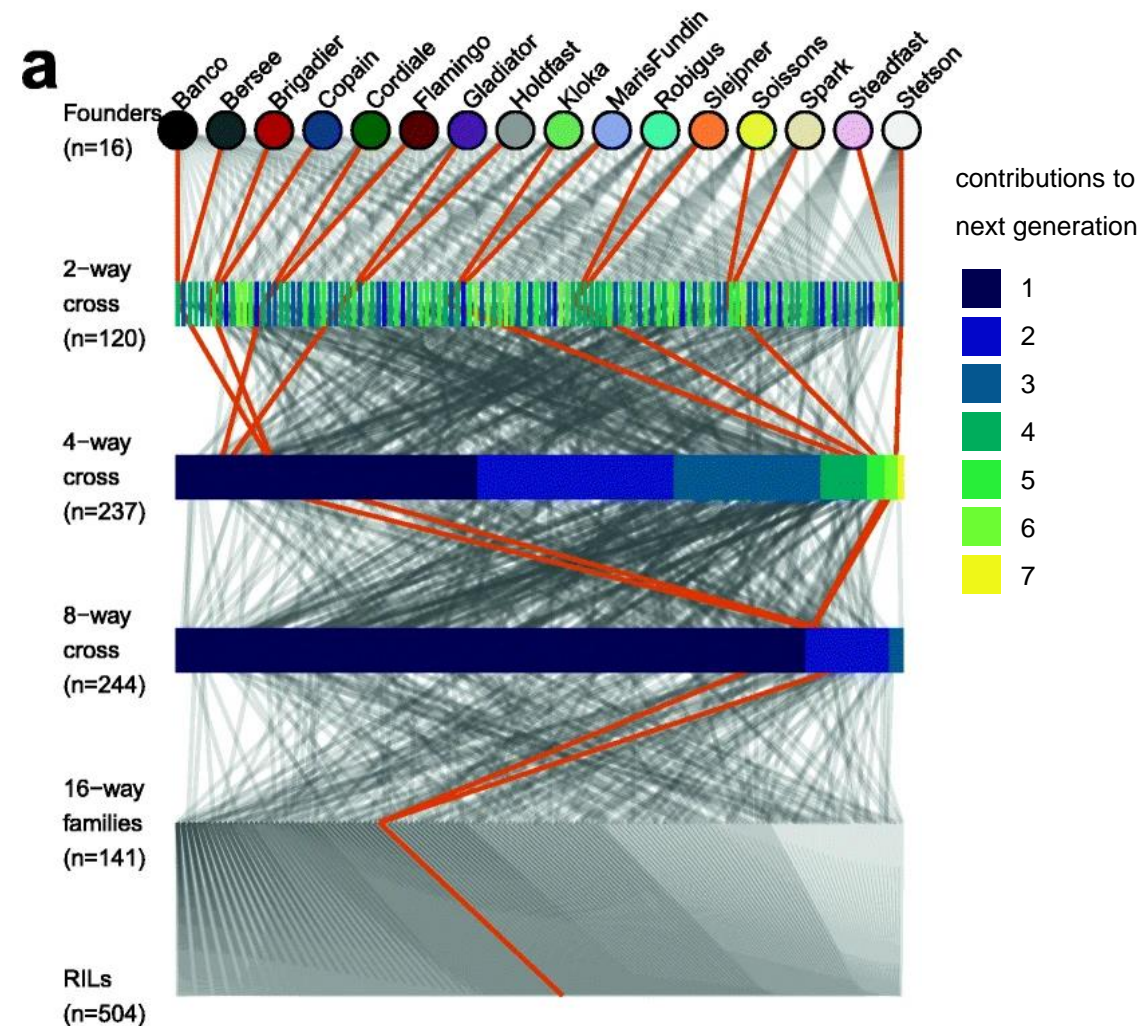
Design types

8 founders, 1 funnel (Basic design)



Cavanagh et al (2008) From mutations to MAGIC: resources for gene discovery, validation and delivery in crop plants

16 founders, 15 funnel (Partial design)



Scott et al (2021) Limited haplotype diversity underlies polygenic trait architecture across 70 years of wheat breeding

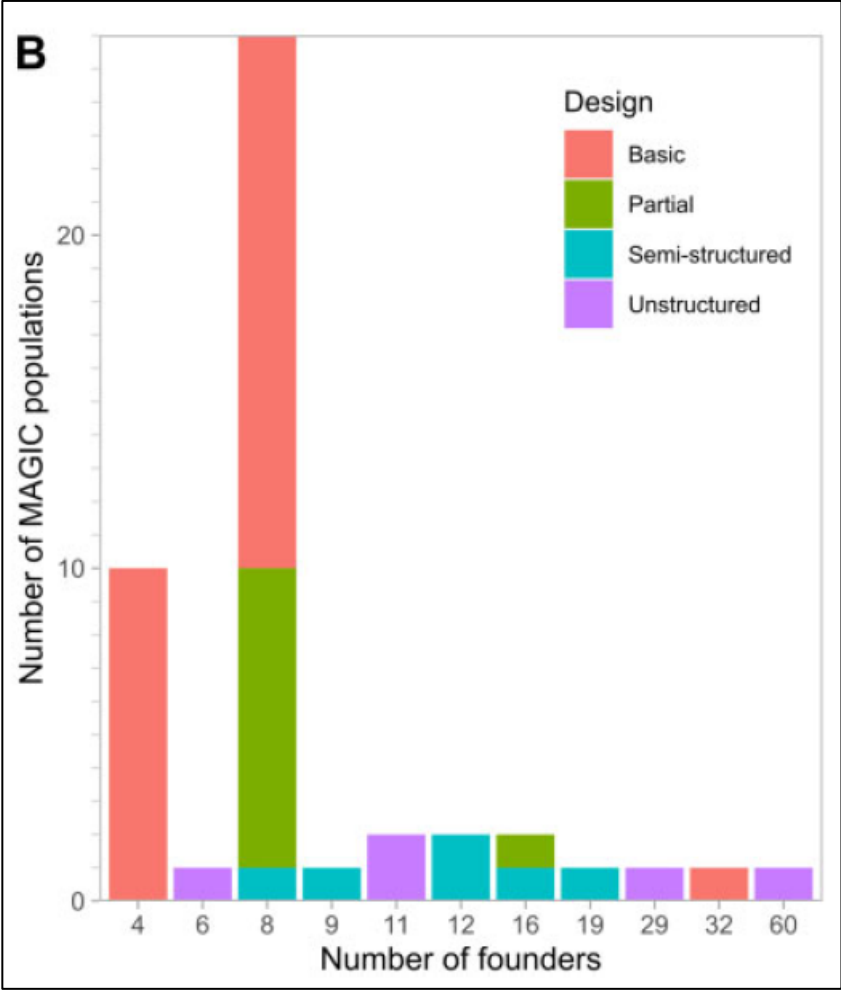
Design classification

Number of funnels
in a full design

$$\frac{n!}{2^{n-1}}$$

- Number of permutations, e.g. AB x CD, CD x AB, AC x BD, ...
- Number of equivalent permutations, e.g. AB x CD = CD x AB, ...

Founders	Funnels
4	3
8	315
16	638,512,875



Design comparison

UK8 (NIAB MAGIC elite)

Founders = A:Alchemy, B:Brompton, C:Claire, D:Hereward,
E:Rialto, F:Robigus, G:Soissons, H:Xi19

2-way = A x B, A x C, ..., G x H (28)

4-way = AB x CD, AB x CE, ..., EF x GH (210)

8-way = ABCD x EFGH, ..., AHFG x BECD (210)

- Elite founders from 1991 to 2006
- 643 RILs

Mackay et al (2014) An Eight-Parent Multiparent Advanced Generation Inter-Cross Population for Winter-Sown Wheat: Creation, Properties, and Validation. G3 4: 1603-1610.

DE8 (WM-800)

Founders = A:Patras, B:Meister, C:Linus, D:JB Asano,
E:Tobak, F:Bernstein, G:Safari, H:Julius

2-way = A x B, C x D, E x F, G x H (4)

4-way = AB x CD, EF x GH (1)

8-way = 9 ABCD x 9 EFGH, 9 EFGH x 9 ABCD (18)

- Elite founders from 2008 to 2017
- 910 RILs

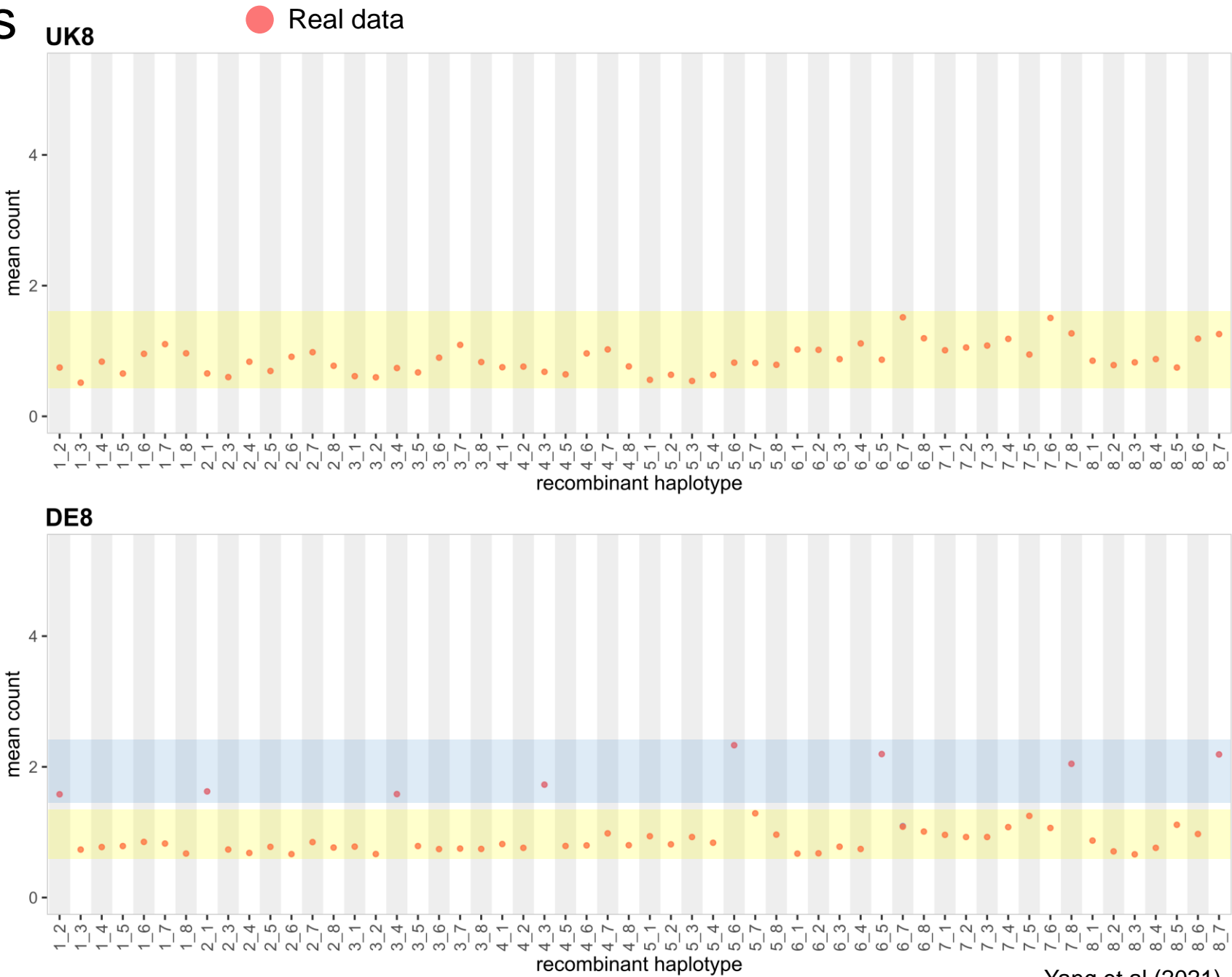
Sannemann et al (2018) Adaptive selection of founder segments and epistatic control of plant height in the MAGIC winter wheat population WM-800. BMC Genom 19:559

Note: Both DE8 and UK8 were genotyped using the same 90k array, so the marker data were filtered down to 5,138 markers in common.

This gave an average of 1.024 cM between two adjacent markers.

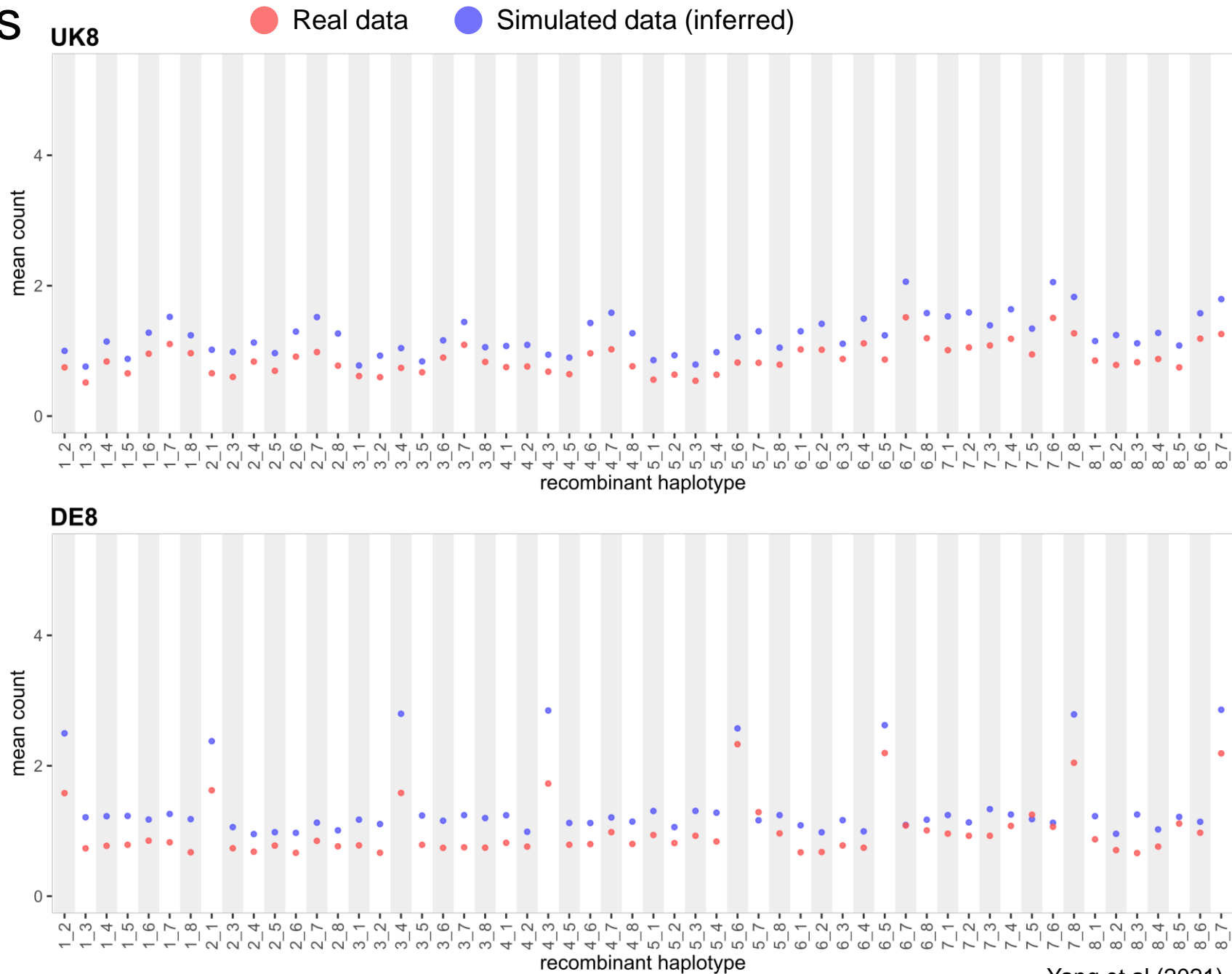
Recombinant haplotypes

- $64 - 8 = 56$ possible recombinant haplotypes (RH) between any two markers
- Bias for two-way RH in DE8 over UK8



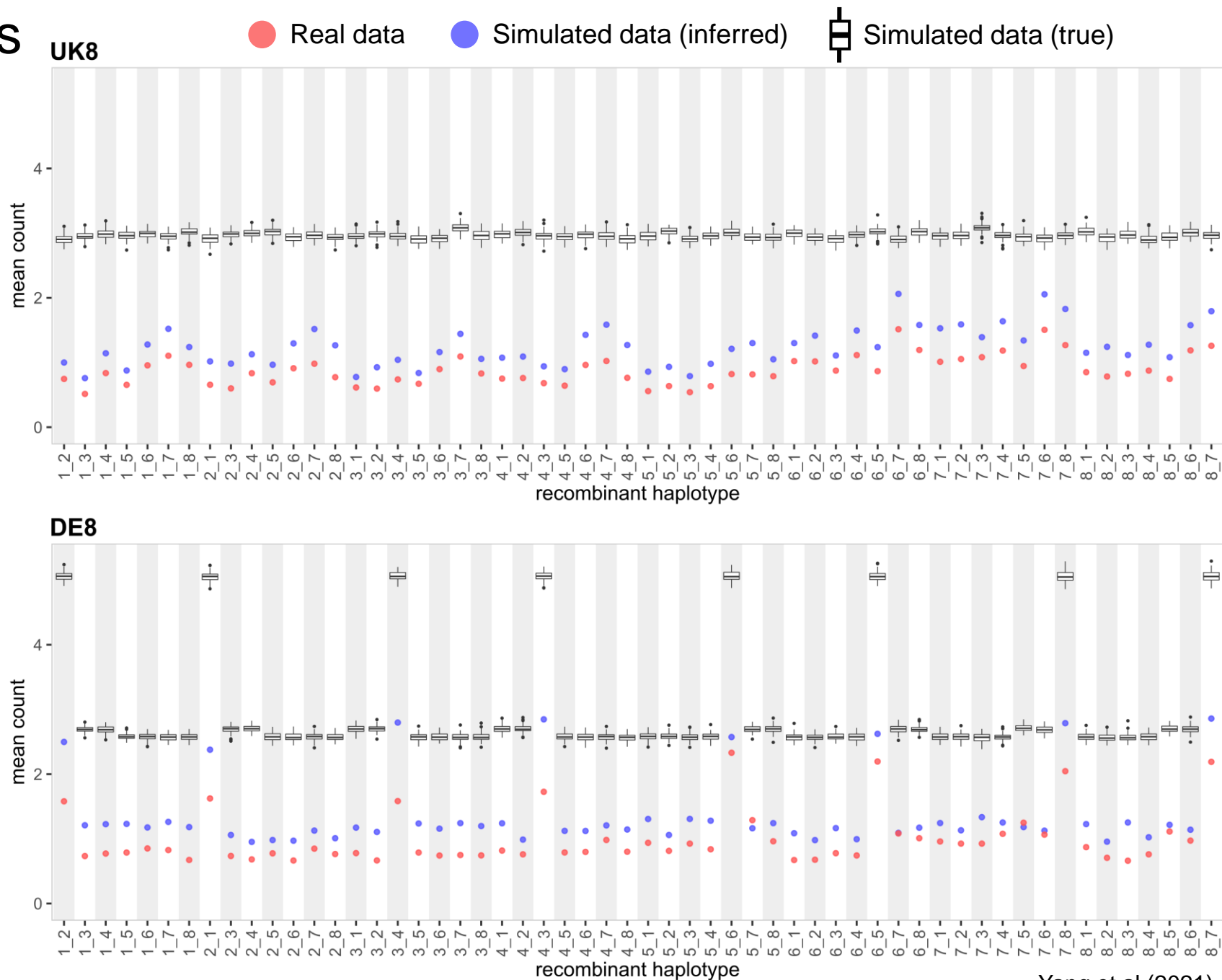
Recombinant haplotypes

- $64 - 8 = 56$ possible recombinant haplotypes (RH) between any two markers
- Bias for two-way RH in DE8 over UK8
- Confirmed by simulation (same pedigree, infer founder haplotypes using R/qtI2)

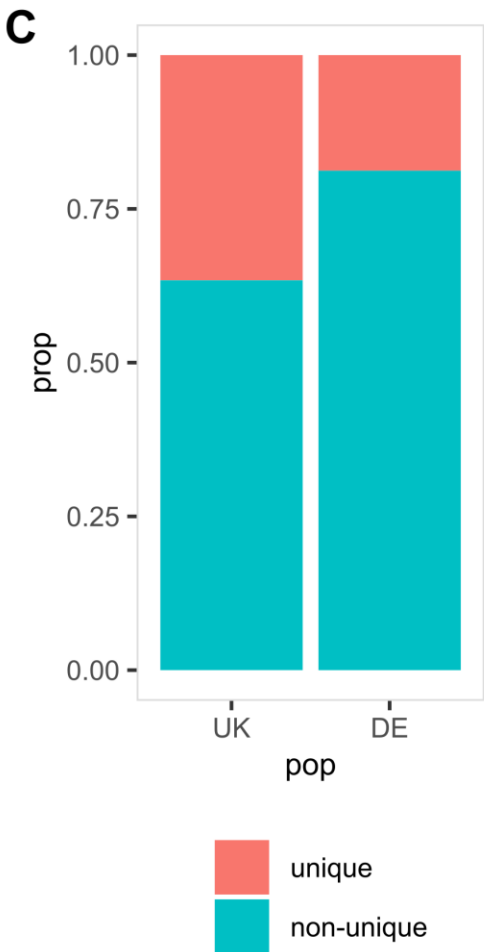
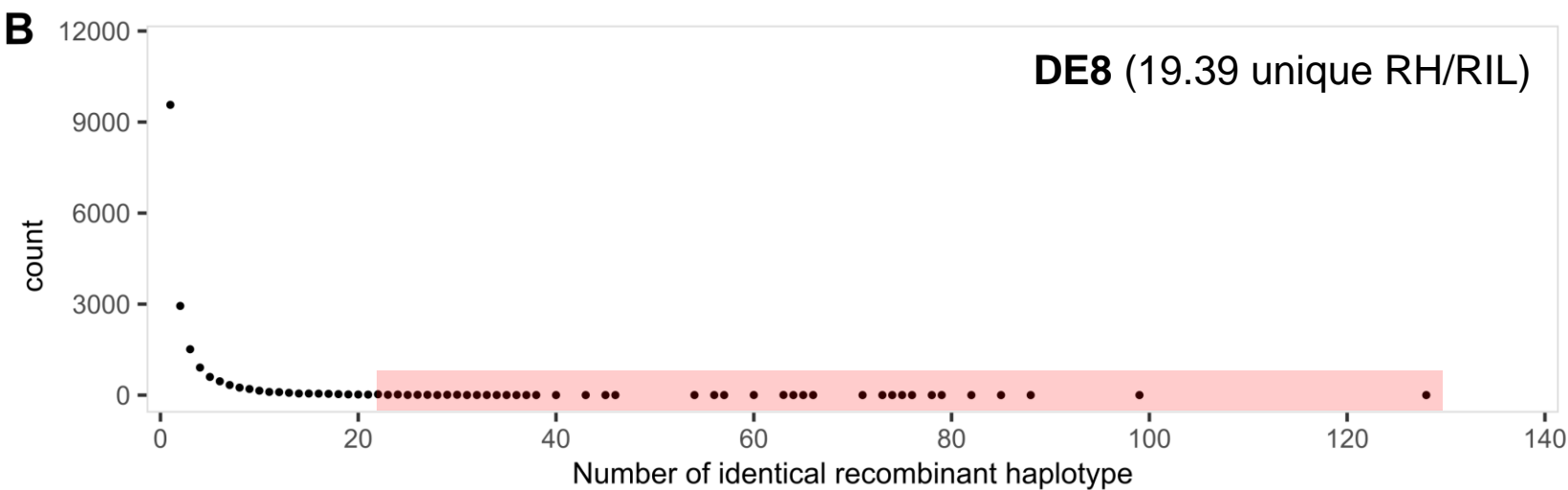
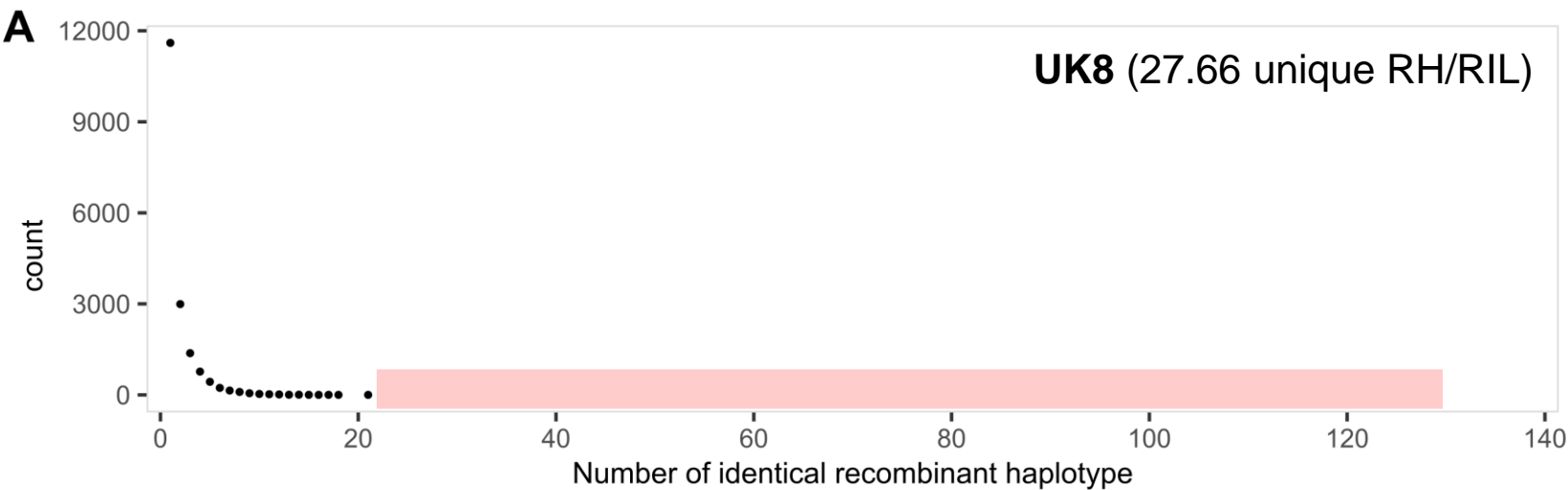


Recombinant haplotypes

- $64 - 8 = 56$ possible recombinant haplotypes (RH) between any two markers
- Bias for two-way RH in DE8 over UK8
- Confirmed by simulation (same pedigree, infer founder haplotypes using R/qtI2)
- True founder genotypes (ignores marker density) suggests only 1/3 RH can be recovered. This can be improved by increasing marker density (not shown here).

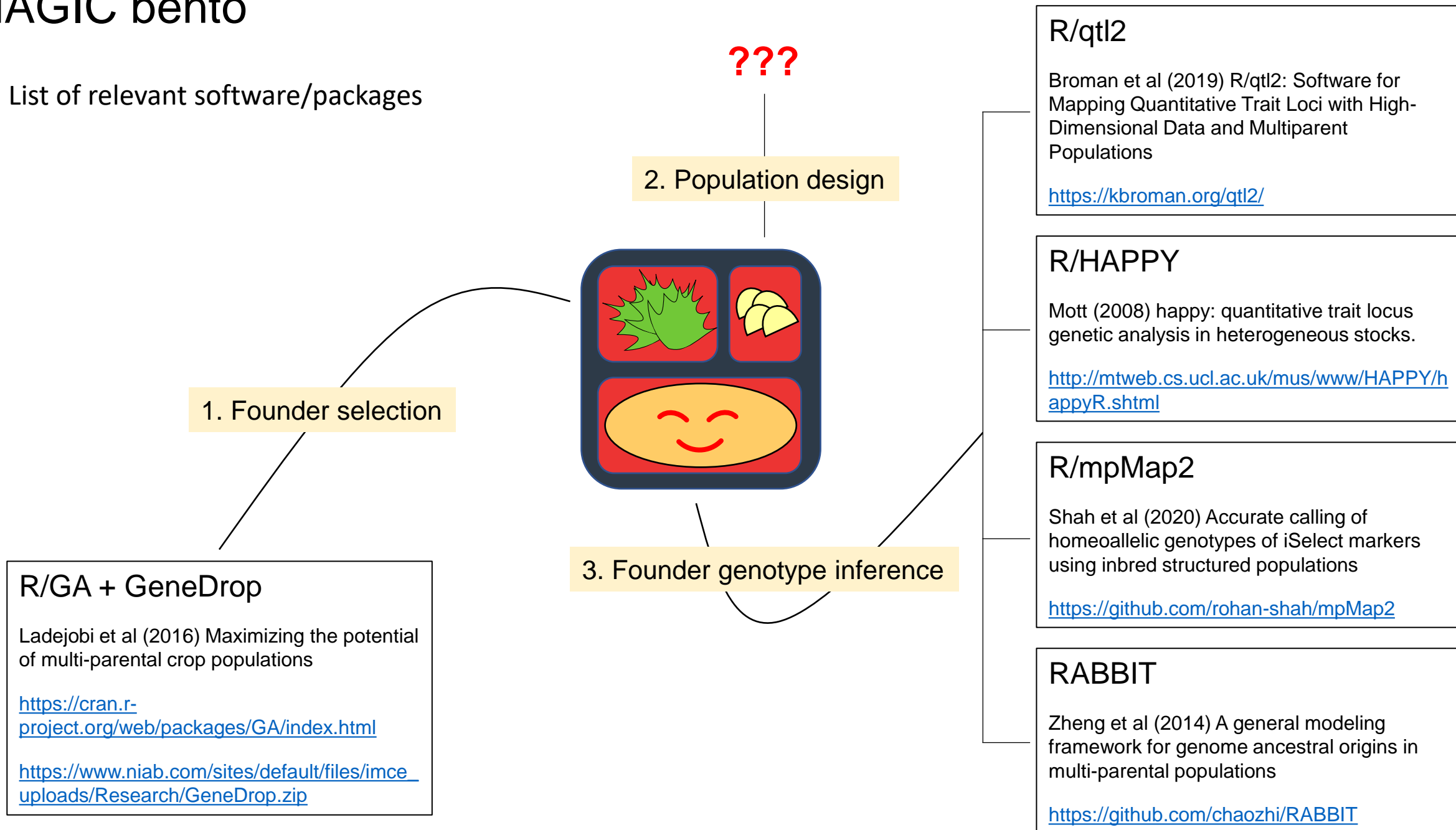


Unique recombinant haplotypes



MAGIC bento

List of relevant software/packages



R/magicdesign for population design

Input method

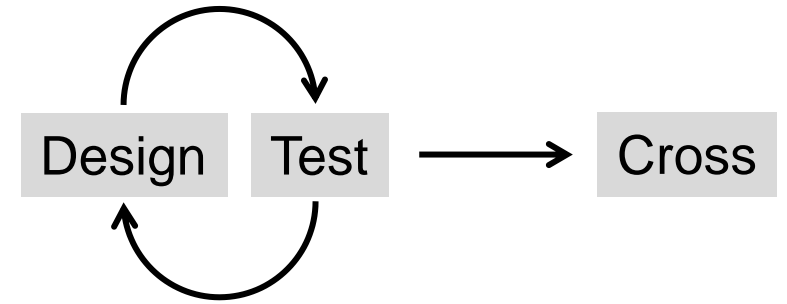
1. Preset parameters, e.g. numbers of funnels, replicates, selfing generations, etc...
2. Custom pedigree, CSV with 4 columns: unique individual ID, parent 1 ID, parent 2 ID and generation number.

Output

1. Summary of crosses.
2. Recombinant haplotype plot.
3. Founder distribution plot.
4. Pedigree.

R package (<https://github.com/cjyang-work/magicdesign>)

R/Shiny app (<https://magicdesign.shinyapps.io/magicdesignee/>)



Step 1: Input (preset parameters)

```
# Basic design
magic.eval(n=8,
          m=0,
          reps=c(1,20,35),
          self=c(0,0,4),
          balanced=FALSE,
          chr.len=seq(1.0, 1.9, 0.1),
          n.sim=50)
```

```
# Partial design
magic.eval(n=8,
          m=1,
          reps=c(1,10,10),
          self=c(0,0,4),
          balanced=TRUE,
          chr.len=seq(1.0, 1.9, 0.1),
          n.sim=50)
```

```
# Partial design + self
magic.eval(n=8,
          m=1,
          reps=c(1,10,10),
          self=c(0,1,4),
          balanced=TRUE,
          chr.len=seq(1.0, 1.9, 0.1),
          n.sim=50)
```

magicdesigner

magicdesigner

Main Designs

Number of founders
8

Number of chromosomes
1

Chromosome names
1

Chr 1
1

Inbred founders
Yes

Number of simulations
1

Marker distance (Morgan)
0.01

Haplotype interval
0.05

Number of haploid marker data to use in evaluation
1

Number of tries (ignored in unbalanced design)
1000

Reset all to defaults

magicdesigner

Main Designs

1 2 3 4 5 6

Balanced design
Yes

Number of funnel sets (min = 1, max = 45)
1

Number of replicates for X-way individuals

2-ways (reps)
1

4-ways (reps)
1

8-ways (reps)
10

Number of generations to self for X-way individuals

2-ways (self)
0

4-ways (self)
0

8-ways (self)
0

Type of extra cross to add
0

Number of replicates for the extra cross individuals
1

Number of generations to self after the extra cross
3

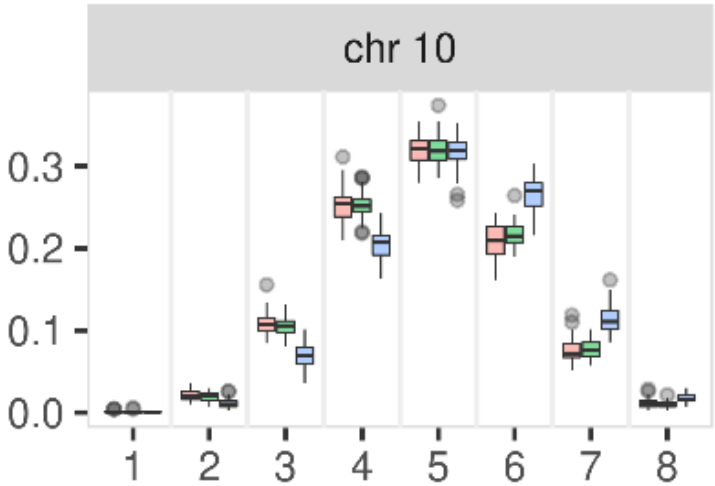
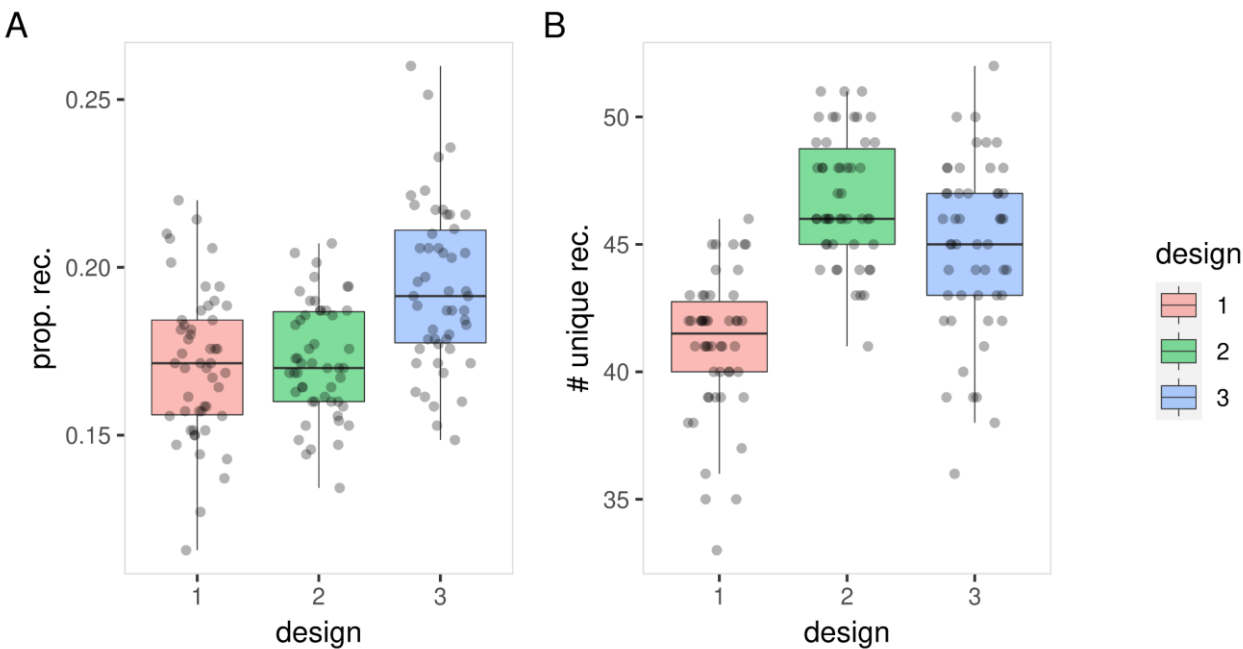
Minimize individuals & crosses
No

Pedigree in CSV format
Browse... No file selected ☒ Header

Run design 1

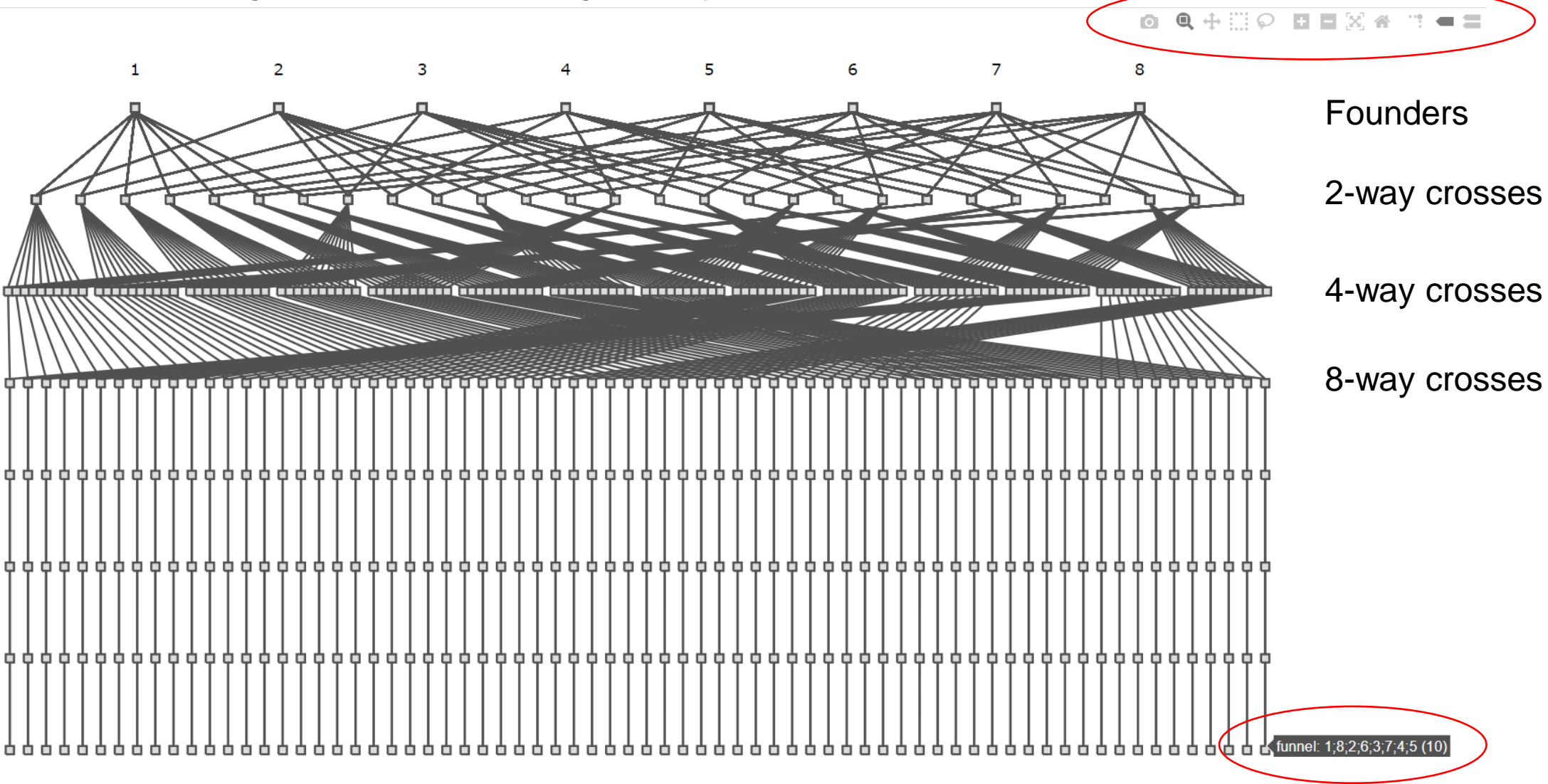
Step 2: Output (results visualization)

	design 1	design 2	design 3
founder	8	8	8
type	basic	partial	partial
reps	1,20,35,0	1,10,10,0	1,10,10,0
self	0,0,4,0	0,0,4,0	0,1,4,0
cross	4,2,20	28,14,70	28,14,70
generation	7	7	8
RIL	700	700	700
funnel	1	7	7



Step 3: Pedigree and crossing scheme

Interactive pedigree in HTML file using R/plotly



Step 3: Pedigree and crossing scheme

Interactive pedigree in HTML file using Riploty

Export as CSV:

- 1. Individual ID
- 2. Parent 1 ID
- 3. Parent 2 ID
- 4. Generation

	A	B	C	D
1	V1	V2	V3	V4
2	1			0
3	2			0
4	3			0
5	4			0
6	5			0
7	6			0
8	7			0
9	8			0
10	1;2_A00	1	2	1
11	1;3_A00	1	3	1
12	1;4_A00	1	4	1
13	1;5_A00	1	5	1
14	1;6_A00	1	6	1
15	1;7_A00	1	7	1
16	1;8_A00	1	8	1
17	4;5_A00	4	5	1

Founders

2-way crosses

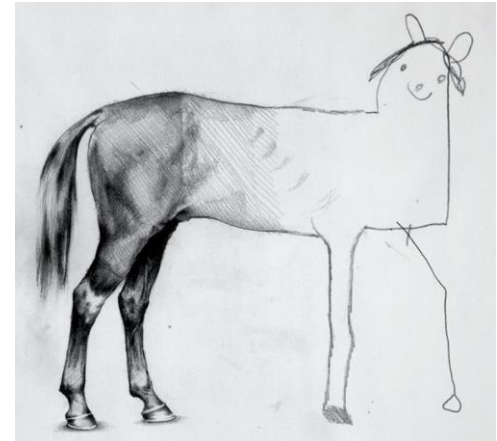
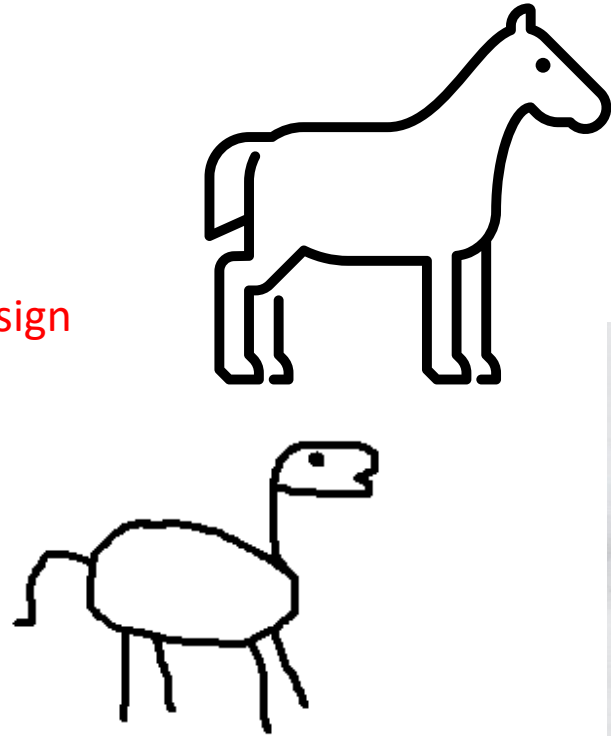
4-way crosses

8-way crosses

Summary

- MAGIC: goals, applications, strengths, weaknesses
- Diversity in population design, recombination landscape
- Plan ahead with R/magicdesign

Choose an appropriate MAGIC population design
for the target species.



The horse by Ali Bati

Acknowledgement

Crafting for a better MAGIC: systematic design and test for Multiparental Advanced Generation Inter-Cross population

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SRUC Principal's Research Group

Wayne Powell

Rajiv Sharma

Ian Mackay

Nicola Rossi

Ian Dawson

David Marshall



R/magicdesign (including the Shiny app)

<https://github.com/cjyang-work/magicdesign>

Slides

<https://github.com/cjyang-work/presentation>

