

QTL mapping in MAGIC populations with R/qlt2

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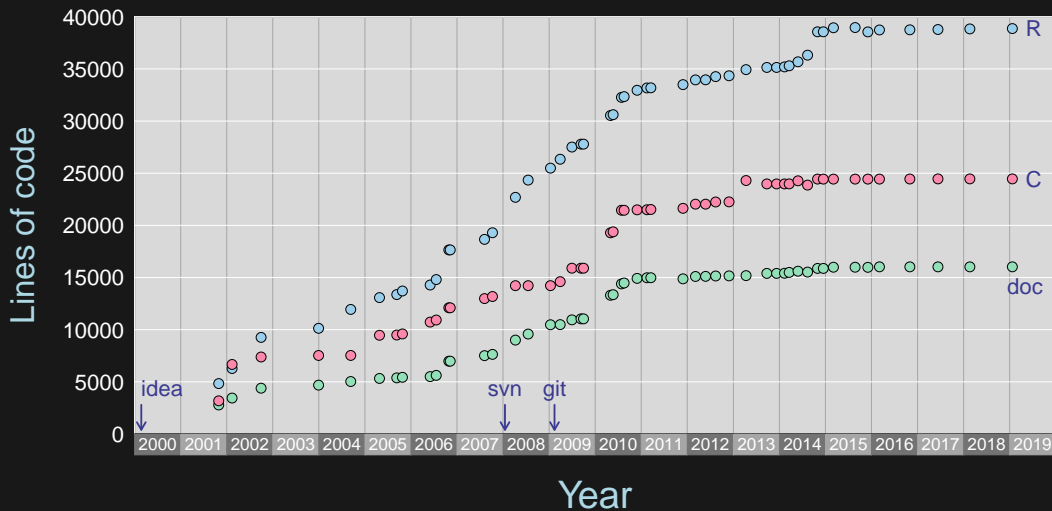
github.com/kbroman

@kwbroman

Slides: bit.ly/MAGIC19



19 years of R/qtl



R/qtl cross types

- ▶ backcross, doubled haploids, haploid
- ▶ intercross
- ▶ 2-way RIL by selfing or sibling mating
- ▶ phase-known 4-way cross



R/qtI2 cross types

- ▶ backcross, doubled haploids, haploid
- ▶ intercross
- ▶ 2-, 4-, 8-, 16-way RIL by selfing
- ▶ 2-, 4-, 8-way RIL by sibling mating
- ▶ 2-, 3-, 8-way advanced intercross
- ▶ 6- and 19-way MAGIC
- ▶ Diversity Outbred (DO) mice
- ▶ F_1 of DO \times inbred
- ▶ general RIL or AIL

Data files

	A	B	C	D	E	F	G
1	id	bolting_days	seed_weight	seed_area	ttl_seedsfruit	branches	height
2	MAGIC.1	15.33	17.15	0.64	45.11	10.5	NA
3	MAGIC.2	22	22.71	0.75	49.11	4.33	42.33
4	MAGIC.3	23	21.03	0.68	57	4.67	50
5	MAGIC.4	18.67	22.45	0.74	54.33	6.33	NA
6	MAGIC.5	18.67	25.36	0.82	38.33	5.67	42.25
7	MAGIC.6	25	21.53	0.71	52	4.33	NA
8	MAGIC.7	15.33	20.92	0.71	39	4	37.35
9	MAGIC.8	14.33	24.2	0.79	50.56	7.33	43.23
10	MAGIC.9	16.33	18.86	0.63	75.78	5.33	42.4
11	MAGIC.10	30	30.46	0.91	56.33	3	48.5
12	MAGIC.11	14	20.58	0.66	41.56	5.67	36.25
13	MAGIC.12	21.33	19.05	0.67	52.33	4.67	49.35
14	MAGIC.14	18.67	21.14	0.72	49.78	6	48.5
15	MAGIC.15	15	21.71	0.73	49	6.33	41.9
16	MAGIC.16	18.33	21.37	0.71	66.67	3.33	18.17

Data files

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1	id	bolting_days	seed_weight	seed_area	ttl_seedsfruit	branches	height	
2		A	B	C	D	E	F	G
3	1	marker	MAGIC.1	MAGIC.10	MAGIC.100	MAGIC.101	MAGIC.102	MAGIC.103
4	2	MN1_29291	A	A	A	B	B	A
5	3	MN1_29716	A	A	A	B	B	A
6	4	MN1_112907	A	A	A	B	B	A
7	5	MASC03771	A	B	A	A	B	A
8	6	MN1_197787	A	B	A	B	B	A
9	7	MN1_340810	A	B	A	A	A	A
10	8	MN1_395107	A	A	A	A	B	A
11	9	MN1_444820	A	A	–	A	A	A
12	10	MN1_494205	A	A	A	A	A	A
13	11	MN1_592863	A	B	A	A	A	A
14	12	MN1_592760	A	A	A	A	A	A
15	13	BKN118	A	A	A	A	A	A
16	14	MN1_1042427	A	B	B	A	B	B
	15	CRY2_1021	A	A	A	A	A	A
	16	CRY2_429	A	A	A	A	B	A

Data files

	A	B	C	D	E	F	G																
1	id	bolting_days	seed_weight	seed_area	tll_seedsfruit	branches	height																
2		A	B	C	D	E	F	G															
3	1	marker	MAGIC.1	MAGIC.10	MAGIC.100	MAGIC.101	MAGIC.102	MAGIC.103															
4	2	1	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	
5	3	2	marker	Bur	Can	Col	Ct	Edi	Hi	Kn	Ler	Mt	No	Oy	Po	Rsch	Sf	Tsu	Wil	Ws	Wu	Zu	
6	4	3	MN1_29291	B	A	A	B	A	A	B	A	A	A	B	B	A	B	A	A	A	A	A	
7	5	4	MN1_29716	B	A	A	B	A	A	B	A	A	A	B	B	A	B	B	A	A	A	A	
8	6	5	MN1_112907	B	A	A	A	B	B	B	B	A	A	B	B	A	B	B	A	A	A	A	
9	7	6	MASC03771	A	B	A	A	B	A	B	A	A	A	A	A	A	A	A	A	A	A	A	
10	8	7	MN1_197787	B	B	A	A	A	B	B	A	A	A	A	A	A	B	A	A	A	B	B	
11	9	8	MN1_340810	B	B	A	B	A	B	A	A	A	A	A	A	A	A	A	A	B	B	A	
12	10	9	MN1_395107	A	A	A	A	A	A	B	A	A	A	A	A	A	A	A	A	A	A	A	
13	11	10	MN1_444820	B	A	A	B	B	A	A	A	A	A	A	A	A	A	B	A	B	B	A	
14	12	11	MN1_494205	B	A	A	A	B	A	A	A	A	A	A	A	A	A	A	A	A	B	A	
15	13	12	MN1_592863	A	B	A	B	A	A	A	B	A	A	A	A	A	A	B	A	B	A	A	
16	14	13	MN1_592760	B	A	A	A	B	A	A	A	A	A	A	A	A	A	A	A	A	A	A	
	15	14	BKN118	B	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	
	16	15	MN1_1042427	A	B	A	B	A	B	B	A	B	A	A	A	B	A	A	B	A	B	A	
		16	CRY2_1021	A	A	A	A	B	A	A	A	A	A	A	A	A	A	A	A	A	A	A	
			CRY2_429	A	A	A	A	A	B	B	B	A	B	A	A	A	A	A	A	B	A	A	
			MASC07014	A	A	B	A	A	A	A	A	A	A	A	A	B	A	A	B	A	A	A	
			MASC03609	A	A	A	A	A	A	B	B	A	B	B	B	A	A	A	A	B	A	A	
			MN1_1296068	A	A	A	A	A	A	B	A	A	A	A	A	A	A	A	A	B	B	A	
			MN1_1399466	A	A	A	A	A	A	B	A	A	A	A	A	A	A	A	-	B	A	A	
			AXR1_381	A	B	A	A	A	B	A	A	A	B	A	A	A	A	A	A	B	A	B	
			MASC07424	A	B	B	A	A	A	A	A	A	A	A	A	A	B	-	A	A	A	A	

Data files

	A		B		C		D		E		F		G										
1	id		bolting_days		seed_weight		seed_area		ttl_seedspruit		branches		height										
2			A		B		C		D		E		F		G								
3	1		marker		MAGIC.1		MAGIC.10		MAGIC.100		MAGIC.101		MAGIC.102		MAGIC.103								
4	2			A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T
5	3		1	marker	Bur	Can	Col	Ct	Edi	Hi	Kn	Ler	Mt	No	Ov	Po	Rsch	Sf	Tsu	Wil	Ws	Wu	Zu
6	4		2	MN1_292			A		B		C			B	A	B	A	A	A	A	A	A	A
7	5		3	MN1_297	1		marker		chr		pos			B	A	B	A	A	A	A	A	A	A
8	6		4	MN1_112	2		MN1_29291		1		0.029291			A	A	A	A	A	A	A	A	A	A
9	7		5	MASC037	3		MN1_29716		1		0.029757			A	A	B	A	A	A	B	B	B	B
10	8		6	MN1_197	4		MN1_112907		1		0.112907			A	A	A	A	A	A	B	B	A	A
11	9		7	MN1_340	5		MASC03771		1		0.174605			A	A	A	A	A	A	A	A	A	A
12	10		8	MN1_444	6		MN1_197787		1		0.197787			A	A	A	B	A	B	B	B	A	A
13	11		9	MN1_494	7		MN1_340810		1		0.34081			A	A	A	A	B	A	B	A	A	A
14	12		10	MN1_592	8		MN1_395107		1		0.395107			A	A	A	A	A	A	A	A	A	A
15	13		11	MN1_592	9		MN1_444820		1		0.444764			A	A	A	A	A	A	A	A	A	A
16	14		12	BKN118	10		MN1_494205		1		0.494205			A	A	A	A	A	A	A	A	A	A
	15		13	CRY2_1021	11		MN1_592863		1		0.592867			A	A	A	A	A	B	A	A	A	A
	16		14	CRY2_429	12		MN1_592760		1		0.592984			A	B	A	A	B	A	A	A	A	A
			15	MASC07014	13		BKN118		1		0.761584			B	A	A	A	A	A	B	A	A	A
			16	MN1_1296068	14		MN1_1042427		1		1.042428			A	A	A	A	A	-	B	A	A	A
				AXR1_309	15		CRY2_1021		1		1.187841			A	A	A	A	A	A	B	A	B	B
				MASC074	16		CRY2_429		1		1.188433			A	A	B	-	A	A	A	A	A	A
					17		MASC07014		1		1.189374												
					18		MASC03609		1		1.22655												
					19		MN1_1296068		1		1.296069												
					20		MN1_1399466		1		1.399467												

Control file (JSON)

```
{
  "description": "Arabidopsis MAGIC data, Gnan et al (2014)",
  "crosstype": "magic19",
  "sep": ",",
  "na.strings": ["-", "NA"],
  "comment.char": "#",
  "geno": "arabmagic_geno.csv",
  "founder_geno": "arabmagic_foundergeno.csv",
  "gmap": "arabmagic_pmap_tair9.csv",
  "pmap": "arabmagic_pmap_tair9.csv",
  "pheno": "arabmagic_pheno.csv",
  "genotypes":
    "A": 3
    "H": 3
    "B": 3
},
"geno_transposed": true,
"founder_geno_transposed": true
}
```

Control file (JSON)

```
{
  "description": "Arabidopsis MAGIC data, Gnan et al (2014)",
  "crosstype": "magic19",
  "sep": ",",
  "na.strings": ["-", "NA"],
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  "geno": "arabmagic_geno.csv",
  "founder_geno": "arabmagic_foundergeno.csv",
  "gmap": "arabmagic_pmap_tair9.csv",
  "pmap": "arabmagic_pmap_tair9.csv",
  "pheno": "arabmagic_pheno.csv",
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  "pmap": "arabmagic_pmap_tair9.csv",
  "pheno": "arabmagic_pheno.csv",
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  "na.strings": ["-", "NA"],
  "comment.char": "#",
  "geno": "arabmagic_geno.csv",
  "founder_geno": "arabmagic_foundergeno.csv",
  "gmap": "arabmagic_pmap_tair9.csv",
  "pmap": "arabmagic_pmap_tair9.csv",
  "pheno": "arabmagic_pheno.csv",
  "genotypes":
    "A": 3
    "H": 3
    "B": 3
  },
  "geno_transposed": true,
  "founder_geno_transposed": true
}
```

Control file (json or yaml)

```
{
  "description": "Arabidopsis MAGIC data, Gnan et al (2014)",
  "crosstype": "magic19",
  "sep": ",",
  "na.strings": ["-", "NA"],
  "comment.char": "#",
  "geno": "arabmagic_geno.csv",
  "founder_geno": "arabmagic_foundergeno.csv",
  "gmap": "arabmagic_pmap_tair9.csv",
  "pmap": "arabmagic_pmap_tair9.csv",
  "pheno": "arabmagic_pheno.csv",
  "genotypes":
    "A": 3
    "H": 3
    "B": 3
},
"geno_transposed": true,
"founder_geno_transposed": true
}
```

Reading data into R

```
library(qtl2)  
arab <- read_cross2("arab_magic.json")
```

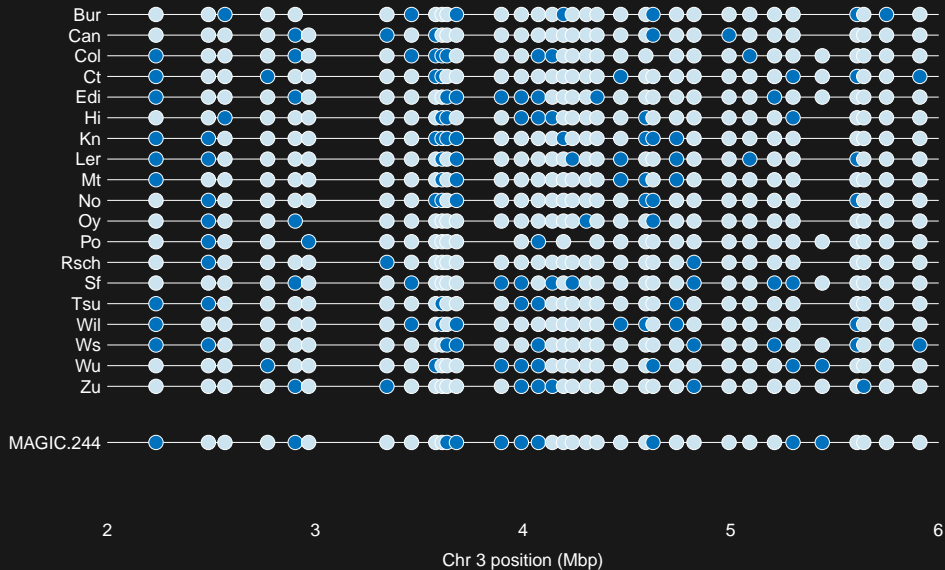
19-way Arabidopsis MAGIC

Kover et al. (2009) PLoS Genet

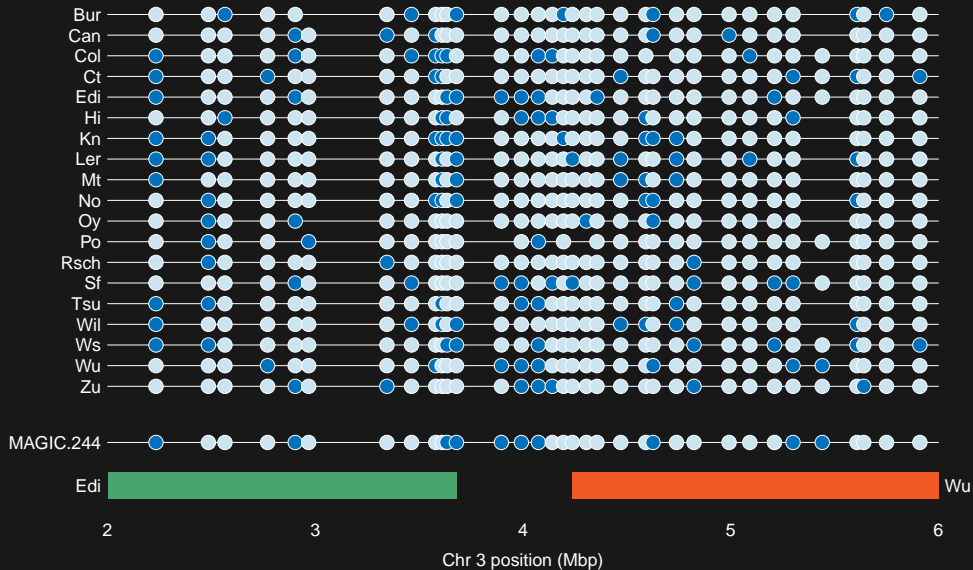
Gnan et al. (2014) Genetics

github.com/rqtl/qtl2data

Genotype reconstruction



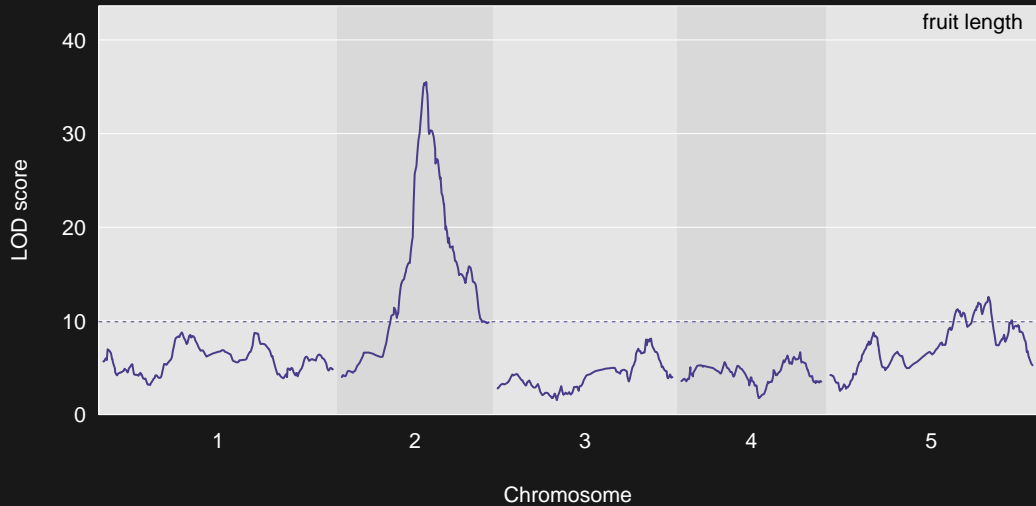
Genotype reconstruction



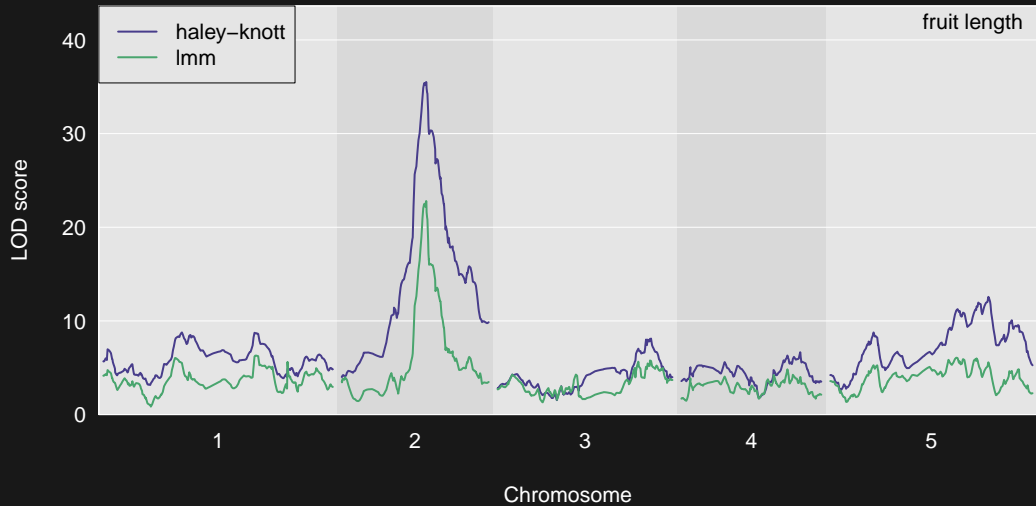
Genotype reconstruction

```
gmap <- insert_pseudomarkers(arab$gmap, step=0.2, stepwidth="max")  
pmap <- interp_map(gmap, arab$gmap, arab$pmap)  
  
pr <- calc_genoprob(arab, gmap, error_prob=0.002, cores=24)
```

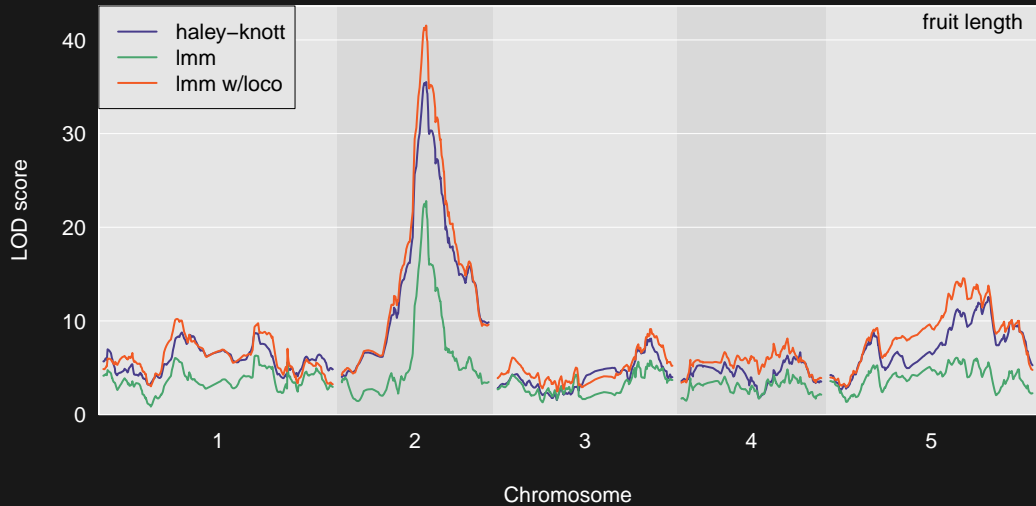
Genome scan



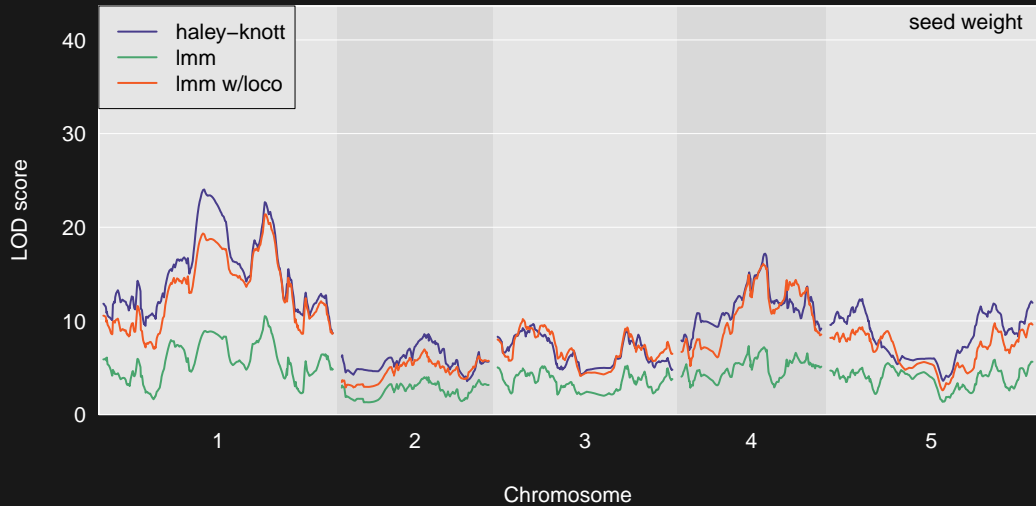
Genome scan



Genome scan



Genome scan



Genome scan

```
out_hk <- scan1(pr, arab$pheno, cores=24)

operm_hk <- scan1perm(pr, arab$pheno, n_perm=1000, cores=24)

k <- calc_kinship(pr, cores=24)
out_lmm <- scan1(pr, arab$pheno, k, cores=24)

k_loco <- calc_kinship(pr, "loco", cores=24)
out_loco <- scan1(pr, arab$pheno, k_loco, cores=24)
```

Future work

- ▶ General treatment of RIL and AIL
- ▶ Treatment of GBS-based genotypes
- ▶ Multiple-QTL models
- ▶ QTL \times environment interactions
- ▶ Interactive data visualization

Slides: bit.ly/MAGIC19



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kbroman.org/qt12

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