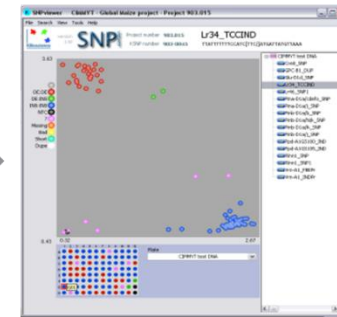
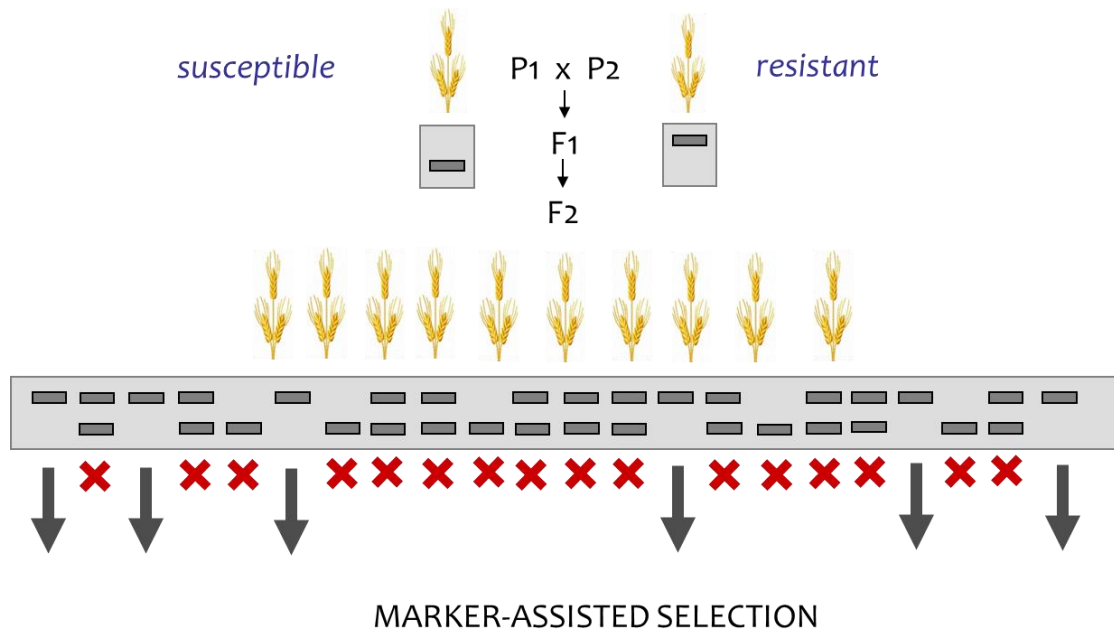


Forward Breeding and Indexed Forward Breeding

Susanne Dreisigacker

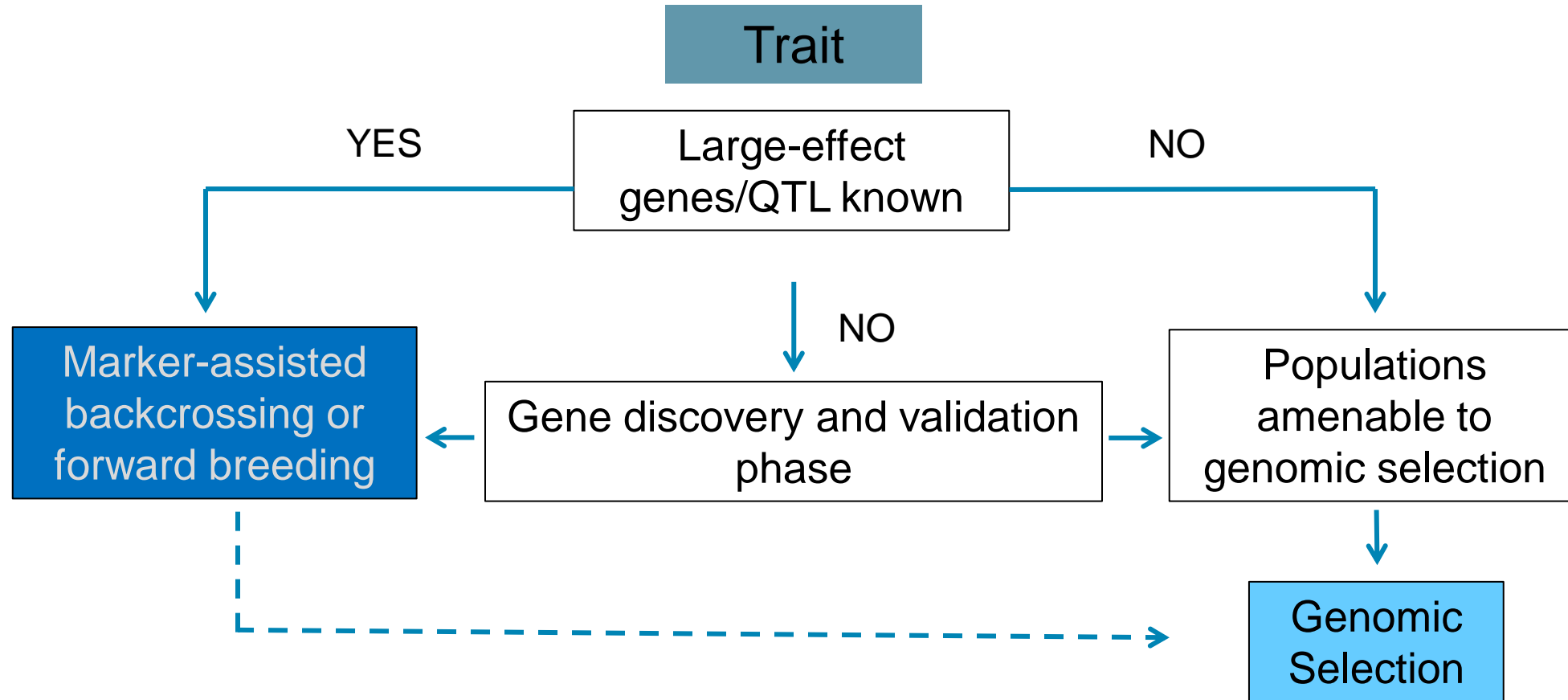
Main Goal of Forward Breeding

To select superior lines in one or several segregating populations based on molecular markers



Genomics-assisted breeding strategies

Forward breeding is mainly used to select large effect genes/QTL



Examples of traits for forward breeding in wheat at CIMMYT

- **Durable adult-plant and race- specific resistance to rusts**
 - Forward breeding to combine of moderately effective slow rusting genes with race specific genes e.g., *Lr34*, *Lr67*, *Lr68*, *Sr2*, *Sr22*, *Sr25*, *Sr35*, *Yr5*, *Yr15*, *Yr57* etc,..
- **Resistance to other disease**
 - Fhb, STB, SB, HF, GB etc,..
- **End-use quality**
 - bread making quality, gluten strength, grain hardness
- **Nutritional quality**
 - grain Zn content, fiber content
- **Growth and development, yield components**
 - TGW, spikelet fertility



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CIMMYT^{MR}

Forward Breeding

Identify lines based on a proportion of favorable alleles (+) at a gene/QTL

Two statistics for each line: **Partial Match** and **Complete Match**

Example: 1 marker per gene/QTL

	QTL 1	QTL 2
	Marker_1	Marker_2
Line_1	+/+	+/+
Line_2	+/+	+/-
Line_3	-/-	-/-

	QTL 1 Partial Match	QTL 2 Partial Match
Line_1	1	1
Line_2	1	0.5
Line_3	0	0

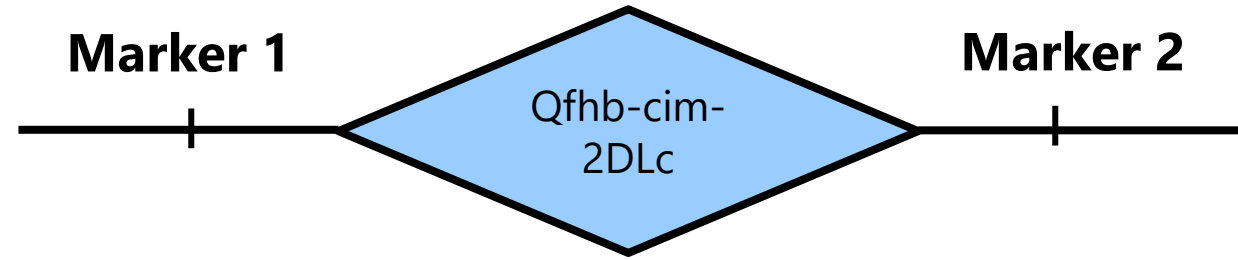
	QTL 1 Complete	QTL 2 Complete
Line_1	1	1
Line_2	1	0.5
Line_3	0	0

Genotypes
Assigned a
Value
+/+ = 1
+/- = 0.5
-/- = 0

Complete
Match =
Minimum of
Assigned
Values

Forward Breeding

Example: 2 markers per gene/QTL



	Qfhb-cim-2DLc	
	Marker_1	Marker_2
Line_1	+/+	+/+
Line_2	+/+	+/-
Line_3	+/+	-/-
Line_4	-/-	-/-

Marker Data

	Qfhb-cim-2DLc	
	Marker_1	Marker_2
Line_1	1	1
Line_2	1	0.5
Line_3	1	0
Line_4	0	0

Genotypes Assigned a Value
 +/+ = 1
 +/- = 0.5
 -/- = 0

	Partial Match
Line_1	1
Line_2	0.75
Line_3	0.5
Line_4	0

Partial Match = Average of Assigned Values

	Complete Match
Line_1	1
Line_2	0.5
Line_3	0
Line_4	0

Complete Match = Minimum of Assigned Values

# ffile = qtl-gobii											
marker_group_name	marker_name	germplasm_group	platform	fav_allele	unfav_allele	fav_allele_trait_name	unfav_allele_trait_name	breeding_value	model	substitution_effect	relative_weight
Lr34	CIMwMAS0052	PT	KASP	C	A	-	Lr34-	YES	additive	5	1
Lr34	CIMwMAS0001	PT	KASP	-	+	Lr34+	Lr34-	YES	additive	-5	1
Lr46	CIMwMAS0094	PT	KASP	A	G	Lr46+	Lr46-	YES	additive	-5	1
Lr68	CIMwMAS0056	PT	KASP	T	C	Lr68+	Lr68-	YES	additive	-7	1
Lr37/Yr17/Sr38	CIMwMAS0004	PT	KASP	T	C	VPM+	VPM-	YES	additive	-5	1
Sr2	CIMwMAS0003	PT	KASP	A	G	Sr2+	Sr2-	YES	additive	-5	1
Fhb1	CIMwMAS0373	PT	KASP	-	+	Fhb1+	Fhb1-	YES	additive	-10	1
Qfhb-cim-2DLc	CIMwMAS0133	PT	KASP	T	C	Mayoor	Ocoroni	YES	additive	-4	1
Qfhb-cim-2DLc	CIMwMAS0137	PT	KASP	A	G	Mayoor	Ocoroni	YES	additive	-4	1

Headers for 'forward breeding'

marker_group_name

shared name for markers for **ONE GENE/QTL**.
E.g., two markers for Lr34.

marker_name

Names must match marker names in genotype file

germplasm_group

Defines the germplasm group the marker belongs to. NOT USED IN ANALYSIS BUT COLUMN MUST BE IN THE FILE

fav_allele

Designation of the favorable allele at the marker. Must match a genotype in the genotype file (ie, C,G,T,A,+)

Analysis Results

Line	Data ...	% Data	Het ...	% Het	Lr34 - Partial Match	Lr46 - Partial M...	Sr2 - ...	Fhb1 ...	Qf h -...	Lr37/...	Lr68 -...	Qf h ...	Lr34 - Complete Match	Lr46 - Complet...	S...	C...	D...
PT20M...	9	100	0	0	0.5	1	0	0	0	1	1	0	0	1	0	0	1	1	0	0
PT20M...	9	100	0	0	0.5	1	0	0	0	1	1	0	0	1	0	0	1	1	0	0
PT20M...	9	100	0	0	0.5	1	0	0	0	1	0	0	0	1	0	0	1	0	0	0
PT20M...	9	100	0	0	0.5	1	0	0	0	1	0	0	0	1	0	0	1	0	0	0
PT20M...	9	100	0	0	0.5	1	0	0	0	0	1	0	0	1	0	0	0	1	0	0
PT20M...	9	100	0	0	0.5	1	0	0	0	1	1	0	0	1	0	0	1	1	0	0
PT20M...	9	100	0	0	0.5	1	0	0	0.5	1	1	0	0	1	0	0	1	1	0	0
PT20M...	9	100	0	0	0.5	1	0	0	0.5	1	0	0	0	1	0	0	1	0	0	0
PT20M...	9	100	0	0	0.5	1	0	0	0.5	1	0	0	0	1	0	0	1	0	0	0
PT20M...	9	100	0	0	0.5	1	1	1	1	1	0	1	0	1	1	1	1	1	0	0	0
PT20M...	9	100	0	0	0.5	1	1	1	1	1	0	1	0	1	1	1	1	1	0	0	0



Indexed Forward Breeding

Uses the breeding values to determine the value of a line

Two statistics for each line: **Molecular Breeding Value** and **Weighted Molecular Breeding Value**

$$MBV_j = \sum_{i=1}^m |S_i| * D_{ij} \quad \text{Molecular Breeding value}$$

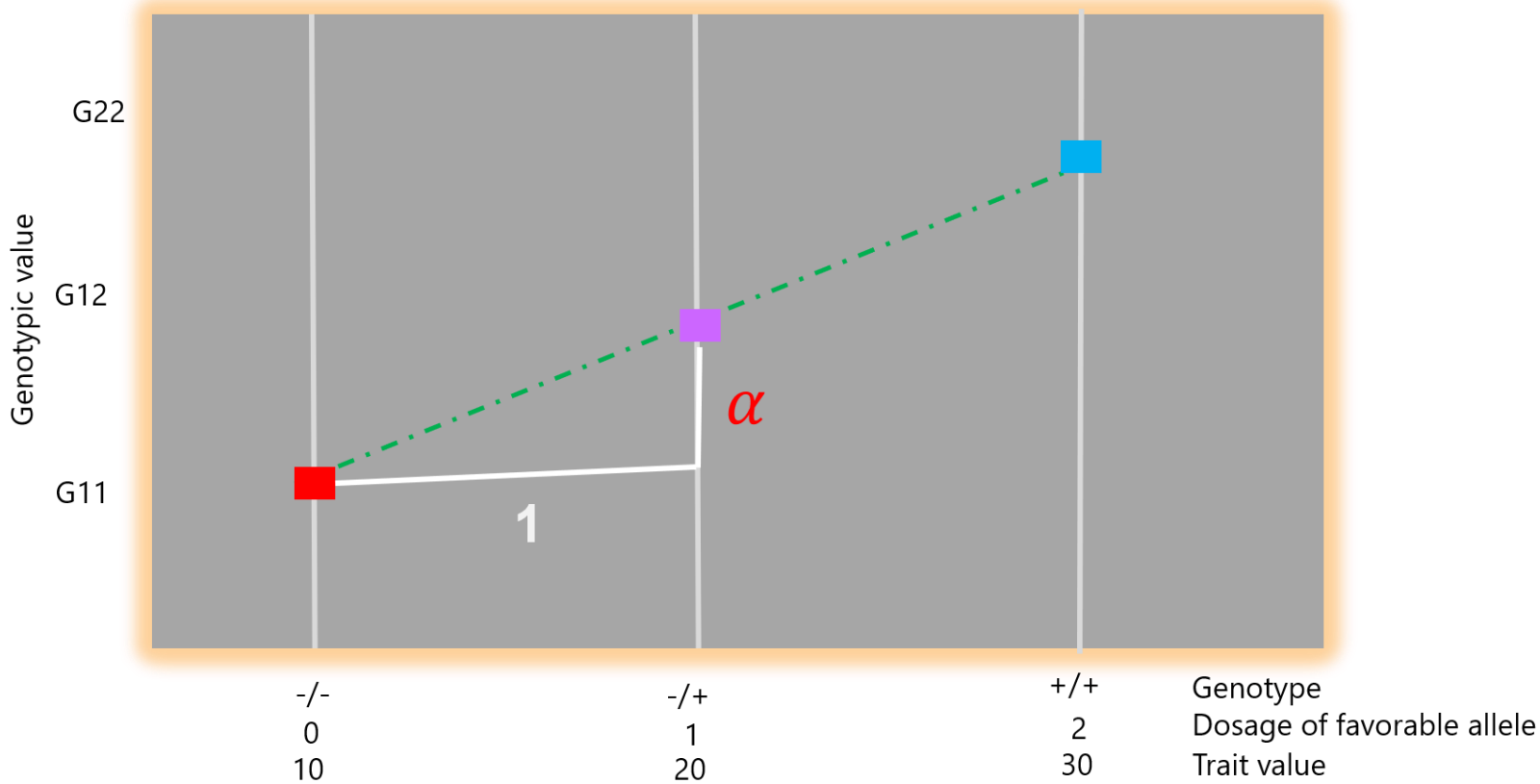
S_i = substitution effect at loci i

D_{ij} = multiplier based on gene action of i^{th} QTL and the genotype of the j^{th} individual

$$wMBV_j = \sum_{i=1}^m w_i * |S_i| * D_{ij} \quad \text{Weighted Molecular Breeding value}$$

w_i = relative weight assigned to i^{th} marker

Substitution effect S_i or a_i



- GWAS / QTL mapping
- Regression – favorable allele dosage on trait

$$y = \mu + \alpha D_i + \varepsilon$$

- R^2 = variance explained as proxy?

the effect of substituting a "+" allele for a "-" allele = 10

Indexed Forward Breeding

$$MBV_j = \sum_1^m |S_i| * D_{ij}$$

S_i = substitution effect at loci i

D_{ij} = multiplier based on gene action of i^{th} QTL and the genotype of the j^{th} individual

	D _i		
	+/+	+/-	-/-
Additive	2	1	0
+ is Dominant	2	2	0
+ is Recessive	2	0	0

# fjfile = qtl-gobii											
marker_group_name	marker_name	germplasm_group	platform	fav_allele	unfav_allele	fav_allele_trait_name	unfav_allele_trait_name	breeding_value	model	substitution_effect	relative_weight
Lr34	CIMwMAS0052	PT	KASP	C	A	-	Lr34-	YES	additive	5	1
Lr34	CIMwMAS0001	PT	KASP	-	+	Lr34+	Lr34-	YES	additive	-5	1
Lr46	CIMwMAS0094	PT	KASP	A	G	Lr46+	Lr46-	YES	additive	-5	1
Lr68	CIMwMAS0056	PT	KASP	T	C	Lr68+	Lr68-	YES	additive	-7	1
Lr37/Yr17/Sr38	CIMwMAS0004	PT	KASP	T	C	VPM+	VPM-	YES	additive	-5	1
Sr2	CIMwMAS0003	PT	KASP	A	G	Sr2+	Sr2-	YES	additive	-5	1
Fhb1	CIMwMAS0373	PT	KASP	-	+	Fhb1+	Fhb1-	YES	additive	-10	1
Qfhb-cim-2DLc	CIMwMAS0133	PT	KASP	T	C	Mayoor	Ocoroni	YES	additive	-4	1
Qfhb-cim-2DLc	CIMwMAS0137	PT	KASP	A	G	Mayoor	Ocoroni	YES	additive	-4	1



disease Resistance, we want lower %

unfav_allele
Designation of the UNfavorable allele at the marker.

fav_allele_trait_name
Character designation of favorable allele

unfav_allele_trait_name
Character designation of UNfavorable allele

breeding_value
Select the markers to be used in calculating a breeding value

model
Additive, Dominant or Recessive value of “+” allele

substitution_effect
Defines the substitution effect; a change in phenotypic value when one unfavorable allele is substituted with one favorable allele

relative_weight
useful for prioritizing across marker groups/QTLs

Molecular Breeding value: Example

marker_group_name	marker_name	breeding_value	model	substitution_effect	relative_weight
Fhb1	m1	YES	Additive	-10	1
Fhb1	m2	YES	Additive	-8	1
Fhb2	m3	YES	Dominant	-3	0.5
Fhb3	m4	YES	Additive	-2	0.5

$$MBV_j = \sum_1^m |S_i| * D_{ij}$$

	Fhb1		Fhb2	Fhb3		Fhb1		Fhb2	Fhb3
	Additive	Additive	Dominant	Additive		Additive	Additive	Dominant	Additive
	m1	m2	m3	m4		m1	m2	m3	m4
a₁	-10	-8	-3	-2		-10	-8	-3	-2
Line_1	+/+	+/+	-/-	+/-	Line_1	2	2	0	1
Line_2	-/-	-/-	+/-	+/+	Line_2	0	0	2	2

} D_i

$$MBV_1 = |a_1|D_{11} + |a_3|D_{31} + |a_4|D_{41} = |-10|*2 + |-3|*0 + |-2|*1 = 22$$

$$MBV_2 = |a_1|D_{12} + |a_3|D_{32} + |a_4|D_{42} = |-10|*0 + |-3|*2 + |-2|*2 = 10$$

Line 1 has resistance score of 22: Worst possible line would have score of zero

Molecular breeding value across multiple traits

marker_group_name	marker_name	breeding_value	model	substitution_effect	relative_weight
Fhb2	m3	YES	Additive	-3	1
Yield1	m6	YES	Additive	5	1
Height1	m7	YES	Additive	-5	1

	Fhb2	Yield1	Height1			Fhb2	Yield1	Height1
	Additive	Additive	Dominant			Additive	Additive	Dominant
	m3	m6	m7			m3	m6	m7
	-3	5	-3			-3	5	-3
Line_1	+/+	+/+	-/-	Line_1	2	2	0	0
Line_2	-/-	-/-	+/-	Line_2	0	0	0.5	0.5

What Units ?
 FHB: %
 Yield: bu/ac
 Height: cm

$$MBV_1 = |a_3|D_{31} + |a_6|D_{61} + |a_7|D_{71} = |-3|*2 + |5|*2 + |-3|*0.5 = 17.5$$

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Weighted Molecular Breeding Value:

$$wMBV_j = \sum_1^m w_i * |S_i| * D_{ij}$$

w_i = Relative weight assigned to i^{th} marker



marker_group_name	marker_name	breeding_value	model	substitution_effect	relative_weight
Fhb1	m1	YES	Additive	-10	1
Fhb1	m2	YES	Additive	-8	1
Fhb2	m3	YES	Dominant	-3	0.5
Fhb3	m4	YES	Additive	-2	0.5

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Molecular Breeding value with missing values (NA)

$$MBV \text{ Non - Missing} = \frac{\text{Sum of BV of genotyped QTL}}{\text{Number of genotyped QTL}}$$

	+/+ = 20	+/+ = 6	+/+ = 4			
	FHB1	FHB2	FHB3	Sum of BV	# QTL	MBV-NM
Line_1	+/+	+/+	+/+	30	3	10
Line_2	+/+	+/+	NA	26	2	13
Line_3	+/+	NA	+/+	14	2	7
Line_4	NA	+/+	+/+	10	2	5
Line_5	NA	NA	+/+	4	1	4
Line_6	NA	+/+	NA	6	1	6
Line_7	+/+	NA	NA	20	1	20

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Analysis Results

Line	Lr34	Lr46	Sr2	Fhb1	Qfh...	Lr3...	Lr68	Molecular Breeding V...	Weighted Molecular Breedin...	Molecular Breeding Value (Non Missing)	Weighted ...	# QTLs ...	Selected	Rank	C...	D...
PT20MSBM...	Lr34-/Lr34-	Lr46...	Sr2-/...	Fhb1...	Ocor...	VPM...	Lr68...	20	20	2.857	2.857	7	<input checked="" type="checkbox"/>	0		<input type="checkbox"/>
PT20MSBM...	Lr34+/Lr34+	Lr46...	Sr2-/...	Fhb1...	Ocor...	VPM...	Lr68...	30	30	4.286	4.286	7	<input checked="" type="checkbox"/>	0		<input type="checkbox"/>
PT20MSBM...	Lr34-/Lr34-	Lr46...	Sr2-/...	Fhb1...	Ocor...	VPM...	Lr68...	20	20	2.857	2.857	7	<input checked="" type="checkbox"/>	0		<input type="checkbox"/>
PT20MSBM...	Lr34+/Lr34+	Lr46...	Sr2-/...	Fhb1...	Ocor...	VPM...	NA	NaN	NaN	5	5	6	<input checked="" type="checkbox"/>	0		<input type="checkbox"/>
PT20MSBM...	Lr34-/Lr34-	Lr46...	Sr2-/...	Fhb1...	Ocor...	VPM...	Lr68...	20	20	2.857	2.857	7	<input checked="" type="checkbox"/>	0		<input type="checkbox"/>



Demo files



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QTL file-gobii

# fjfile = qtl-gobii											
marker_group_name	marker_name	germplasm_group	platform	fav_allele	unfav_allele	fav_allele_trait_name	unfav_allele_trait_name	breeding_value	model	substitution_effect	relative_weight
Lr34	CIMwMAS0052	PT	KASP	C	A	-	Lr34-	YES	additive	5	1
Lr34	CIMwMAS0001	PT	KASP	-	+	Lr34+	Lr34-	YES	additive	-5	1
Lr46	CIMwMAS0094	PT	KASP	A	G	Lr46+	Lr46-	YES	additive	-5	1
Lr68	CIMwMAS0056	PT	KASP	T	C	Lr68+	Lr68-	YES	additive	-7	1
Lr37/Yr17/Sr38	CIMwMAS0004	PT	KASP	T	C	VPM+	VPM-	YES	additive	-5	1
Sr2	CIMwMAS0003	PT	KASP	A	G	Sr2+	Sr2-	YES	additive	-5	1
Fhb1	CIMwMAS0373	PT	KASP	-					additive	-10	1
Qfhb-cim-2DLc	CIMwMAS0133	PT	KASP	T					additive	-4	1
Qfhb-cim-2DLc	CIMwMAS0137	PT	KASP	A					additive	-4	1

map file

# fjfile = map		
CIMwMAS0094	1B	670233714
CIMwMAS0133	2D	574351998
CIMwMAS0137	2D	571201794
CIMwMAS0052	7D	47418827
CIMwMAS0001	7D	47413697
CIMwMAS0056	7B	740039652
CIMwMAS0003	3B	8513532
CIMwMAS0373	3B	8528404
CIMwMAS0004	3B	693339706



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Genotypic data

SampleID	GID	Pedigree	CIMwMAS 0094	CIMwMAS 0056	CIMwMAS 0004	CIMwMAS 0003	CIMwMAS 0373	CIMwMAS 0133	CIMwMAS 0137	CIMwMAS 0001	CIMwMAS 0052
PT20MSBM000059	8823465	CMH79A.955/4/AGA/3/4*SN64/CNO67//INIA66/5/NAC/6/RIALTO/7/SOKOLL/WBLL1	A:A	T:T	T:T	G:G	++	T:T	G:G	++	C:C
PT20MSBM000060	8823424	CMH79A.955/4/AGA/3/4*SN64/CNO67//INIA66/5/NAC/6/RIALTO/7/SOKOLL/WBLL1	A:A	T:T	T:T	G:G	++	C:C	G:G	++	C:C
PT20MSBM000061	8823426	CMH79A.955/4/AGA/3/4*SN64/CNO67//INIA66/5/NAC/6/RIALTO/7/SOKOLL/WBLL1	A:A	T:T	T:T	G:G	++	T:T	G:G	++	C:C
PT20MSBM000062	8823427	CMH79A.955/4/AGA/3/4*SN64/CNO67//INIA66/5/NAC/6/RIALTO/7/SOKOLL/WBLL1	A:A	C:C	T:T	G:G	++	T:T	G:G	++	C:C
PT20MSBM000063	8823432	CMH79A.955/4/AGA/3/4*SN64/CNO67//INIA66/5/NAC/6/RIALTO/7/SOKOLL/WBLL1	A:A	T:T	T:T	G:G	++	C:C	G:G	++	C:C
PT20MSBM000064	8823439	CMH79A.955/4/AGA/3/4*SN64/CNO67//INIA66/5/NAC/6/RIALTO/7/SOKOLL/WBLL1	A:A	C:C	T:T	G:G	++	C:C	G:G	++	C:C
PT20MSBM000065	8823445	CMH79A.955/4/AGA/3/4*SN64/CNO67//INIA66/5/NAC/6/RIALTO/7/SOKOLL/WBLL1	A:A	C:C	T:T	G:G	++	C:C	G:G	++	C:C
PT20MSBM000066	8823446	CMH79A.955/4/AGA/3/4*SN64/CNO67//INIA66/5/NAC/6/RIALTO/7/SOKOLL/WBLL1	A:A	C:C	T:T	A:A	--	T:T	A:A	++	C:C
PT20MSBM000067	8823449	CMH79A.955/4/AGA/3/4*SN64/CNO67//INIA66/5/NAC/6/RIALTO/7/SOKOLL/WBLL1	A:A	C:C	T:T	A:A	--	T:T	A:A	++	C:C
PT20MSBM000068	8823452	CMH79A.955/4/AGA/3/4*SN64/CNO67//INIA66/5/NAC/6/RIALTO/7/SOKOLL/WBLL1	A:A	C:C	T:T	G:G	++	C:C	G:G	++	C:C
PT20MSBM000069	8823456	CMH79A.955/4/AGA/3/4*SN64/CNO67//INIA66/5/NAC/6/RIALTO/7/SOKOLL/WBLL1	A:A	C:C	T:T	G:G	++	T:T	G:G	++	C:C
PT20MSBM000070	8823460	CMH79A.955/4/AGA/3/4*SN64/CNO67//INIA66/5/NAC/6/RIALTO/7/SOKOLL/WBLL1	A:A	T:T	C:C	G:G	++	C:C	G:G	++	C:C
PT20MSBM000071	8823461	CMH79A.955/4/AGA/3/4*SN64/CNO67//INIA66/5/NAC/6/RIALTO/7/SOKOLL/WBLL1	A:A	T:T	T:T	G:G	++	C:C	G:G	++	C:C
PT20MSBM000205	8931731	OPATA//SORA/AE.SQUARROSA (323)/4/PIHA//WORRAKATTA/2*PASTOR/3/PRL/2*PASTOR	A:A	C:C	C:C	G:G	++	T:T	G:G	--	C:C
PT20MSBM000206	8931734	OPATA//SORA/AE.SQUARROSA (323)/4/PIHA//WORRAKATTA/2*PASTOR/3/PRL/2*PASTOR	A:A	C:C	C:C	G:G	++	T:T	A:A	--	C:C
PT20MSBM000207	8931735	OPATA//SORA/AE.SQUARROSA (323)/4/PIHA//WORRAKATTA/2*PASTOR/3/PRL/2*PASTOR	A:A	C:C	C:C	G:G	++	T:T	G:G	++	C:C
PT20MSBM000208	8931736	OPATA//SORA/AE.SQUARROSA (323)/4/PIHA//WORRAKATTA/2*PASTOR/3/PRL/2*PASTOR	A:A	C:C	C:C	G:G	++	T:T	A:A	--	C:C
PT20MSBM000209	8931737	OPATA//SORA/AE.SQUARROSA (323)/4/PIHA//WORRAKATTA/2*PASTOR/3/PRL/2*PASTOR	A:A	C:C	C:C	G:G	++	T:T	G:G	++	C:C

Germplasm: 36 bread wheat lines, 4 populations

Markers: 9 KASP markers related to diseases



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