

Identifying and exploiting natural variation

New methods of fine mapping:

- association mapping
- MAGIC

Methods for increasing diversity:

- synthetic wheat



Advantages of new methods for fine mapping

More efficient MAS:

- tag genes not intervals

- some QTL are > 1 gene:

- identification of key rare recombination events

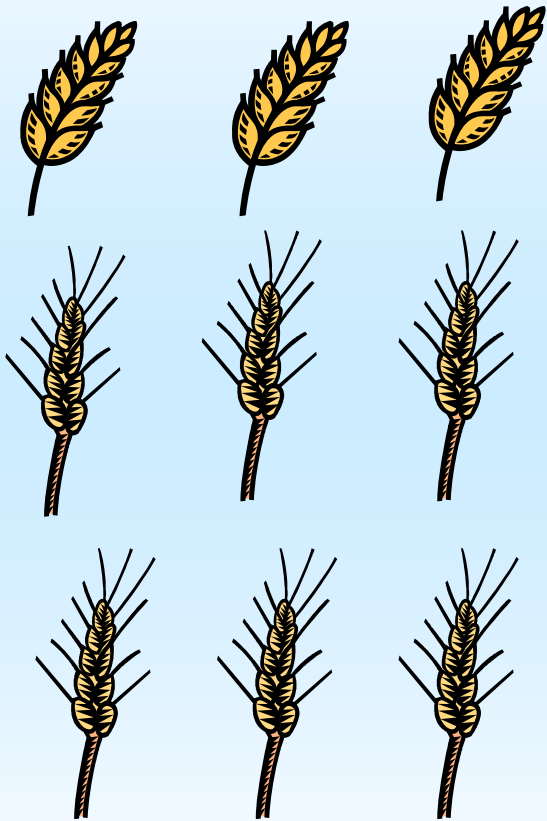
Better detection and modelling of multiple interacting traits and genes.

Identification of gene or QTN will lead to better functional studies.

More applicable to breeders germplasm.

Association mapping is simple

Allele A



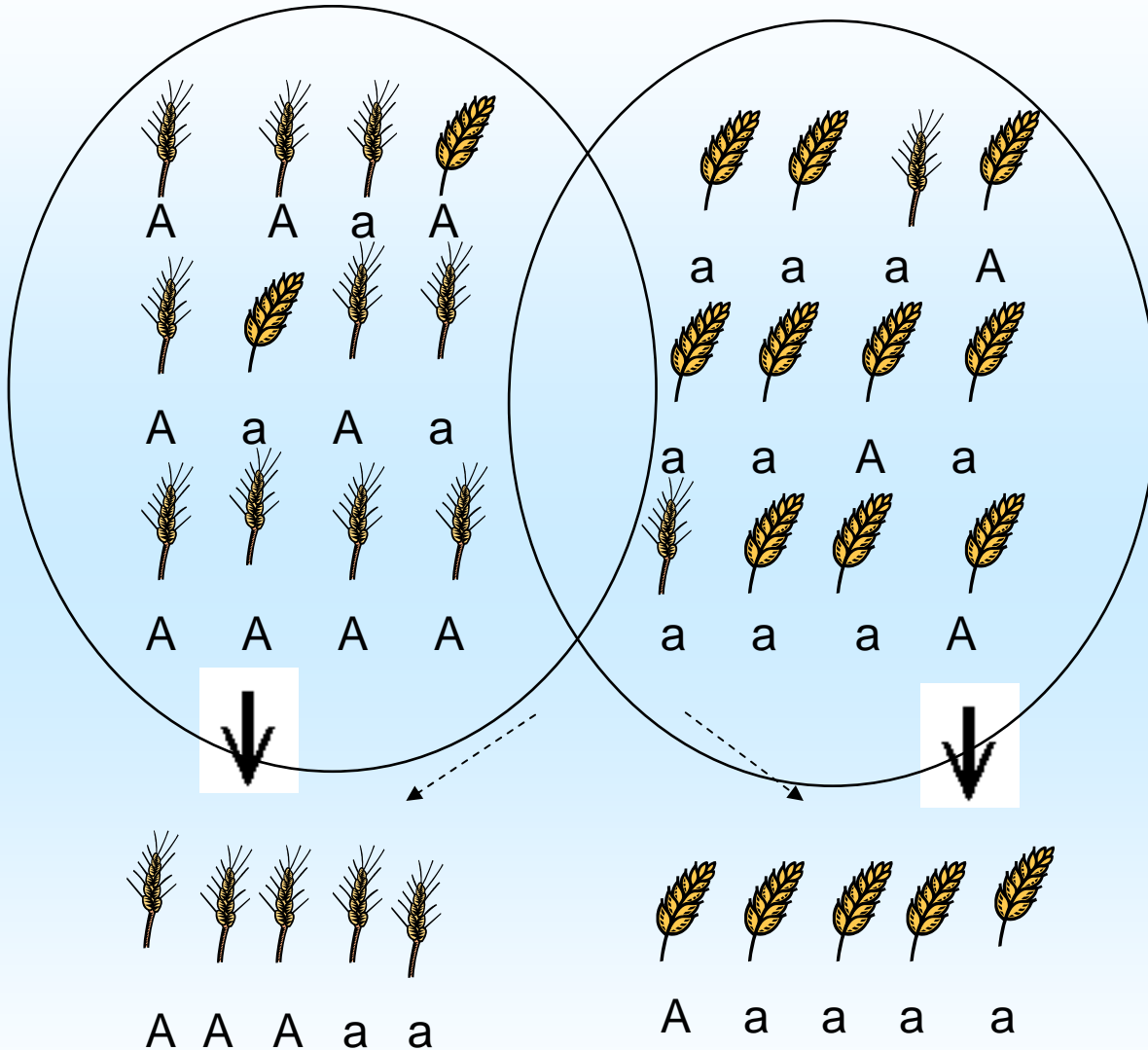
Allele a



Allele a is found more frequently with



Population structure and association



If there are unknown subgroups,

if allele freqs differ between subgroups,

if traits differ between subgroups,

then:

spurious association will be observed.

Relationships among varieties cause false positives too.



Solutions:

Old, design based: family based linkage analysis.

New, analysis based: mapping in diverse populations.

Technology driven: require many molecular markers

An active area of research.



Association vs linkage

Power versus precision

	LD mapping	linkage analysis
Power to detect QTL	low	high
Precision of location	high	low

Therefore: we need both

MAGIC

Multiparent

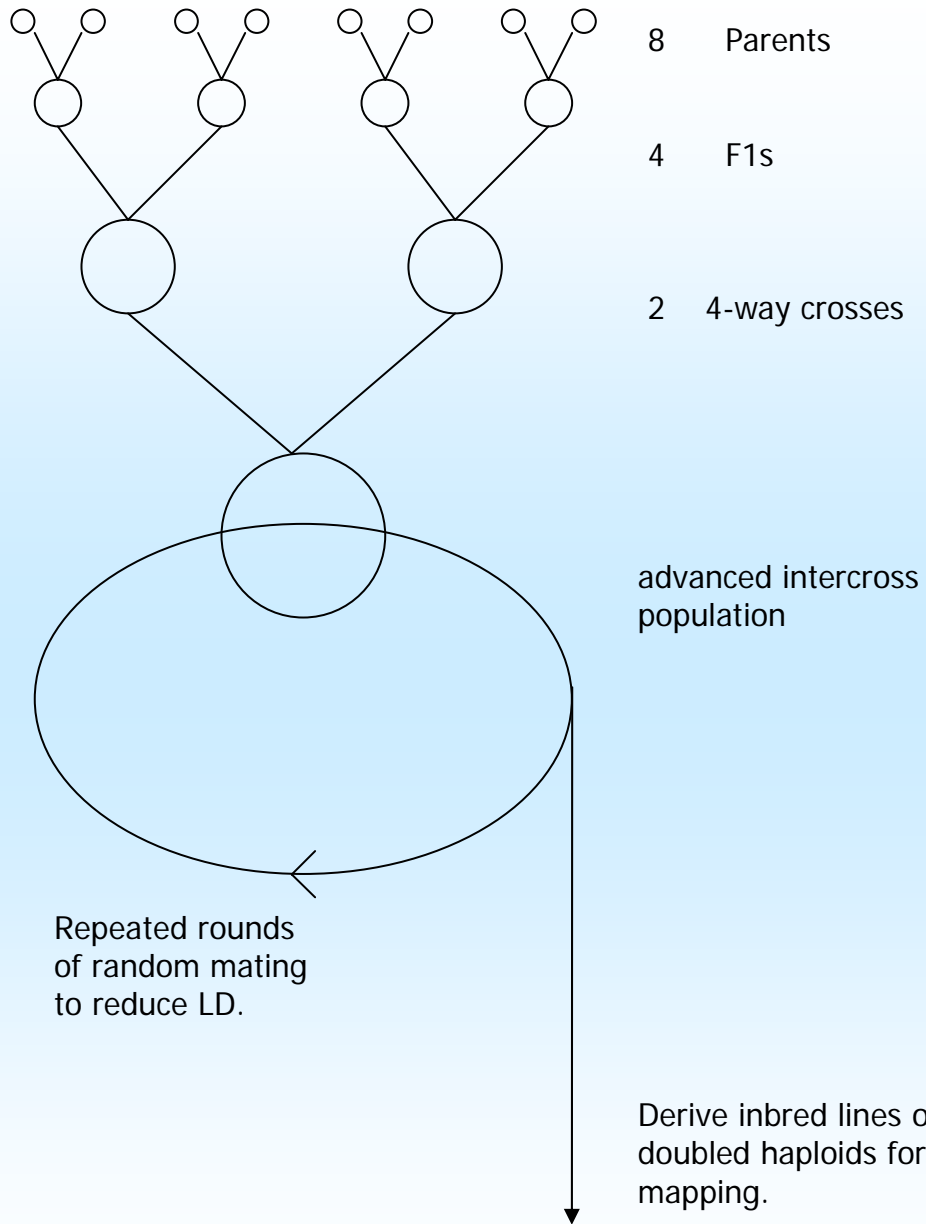
Advanced

Generation

Inter-

Cross

A compliment to both family based linkage analysis and to association testing



MAGIC

Diverse: good for multiple interacting traits and loci.

QTL detection in early generations

Fine mapping in later generations



The Collaborative Cross

Mouse genetics and mouse models of human disease are extremely important in medical and pharmaceutical research.

\$3.5m p.a. for 8 years + \$3m for genotyping.

<http://www.complextait.org/>

“Ideal resource for systems biology as it will provide a reproducible, highly varied yet controlled set of genetic backgrounds for functional genomic studies.”

Success in mouse

97 traits

843 QTLs, average 95% confidence interval of 2.8 Mb.

The QTLs contribute to variation in 97 traits, including models of human disease (asthma, type 2 diabetes mellitus, obesity and anxiety) as well as immunological, biochemical and hematological phenotypes

- 4.8 Mb region with QTL for anxiety

- Select conserved regions and compare sequence distribution pattern among founders with that of the QTN

- 14 SNPs identified as functional candidates out of 15,000

Wheat, MAGIC, NIAB/JIC/INRA

BBSRC/CSI funded for 5 years

2 new populations

1 diverse 16 founders

1 elite 8 founders

2 outbred populations (gms)

less controlled but ready to go

(in collaboration with JIC and INRA)

MAGIC winter wheat populations

diversity

Holfast
 Steadfast
 Banco
 Staring
 Gladiator
 Flamingo
 Kloka
 Cama
 Maris Fundin
 Copain
 Stetson
 Slejpner
 Cordiale
 Bersee
 Brigadier
 Soissons

elite

Hereward
Soissons
Claire
Robigus
 Brigadier
Alchemy
 Xi19
Rialto

reason for choice

quality
 quality, early, diversity
 yield, resistance
 diversity, yield, Rht1, resistance, breeding use
 yield, disease resistance, breeding use
 quality, facultative Sp type, breeding use
 1RS

Bold: parent of publicly available mapping population

INRA outbred population

Established for French pop. gen. studies

12 generations of gms facilitated crossing
60 founders

UK	11
France	15
Other Euro inc. USSR	12
USA	11
other	11

Unique resource, world-wide.

Elm Farm /JIC outbred population

Established for low input/organic breeding

Bezostaya	Buchan
Cadenza	Claire
Deben	Hereward
High Tillering Line (PBI)	Maris Widgeon
Mercia	Monopol
Norman	Option
Pastiche	Pegassos
Renan	Renesansa
Soissons	Spark
Tanker	Thatcher
Wembley	Xi19

4 generations gms facilitated outcrossing

Strengths and weaknesses of methods.

	Linkage	LD	MAGIC
Suitability for fine mapping	-	+	+
Suitability for coarse mapping	+	-	+
Low genotyping requirement	+	-	.
Low phenotype requirement	-	+	-
Resistant to pop. structure	+	-	+
Relevance to breeders	-	+	+
Relevance over time	-	+	+
Time to set up	.	+	-
Score	-1	+2	+5

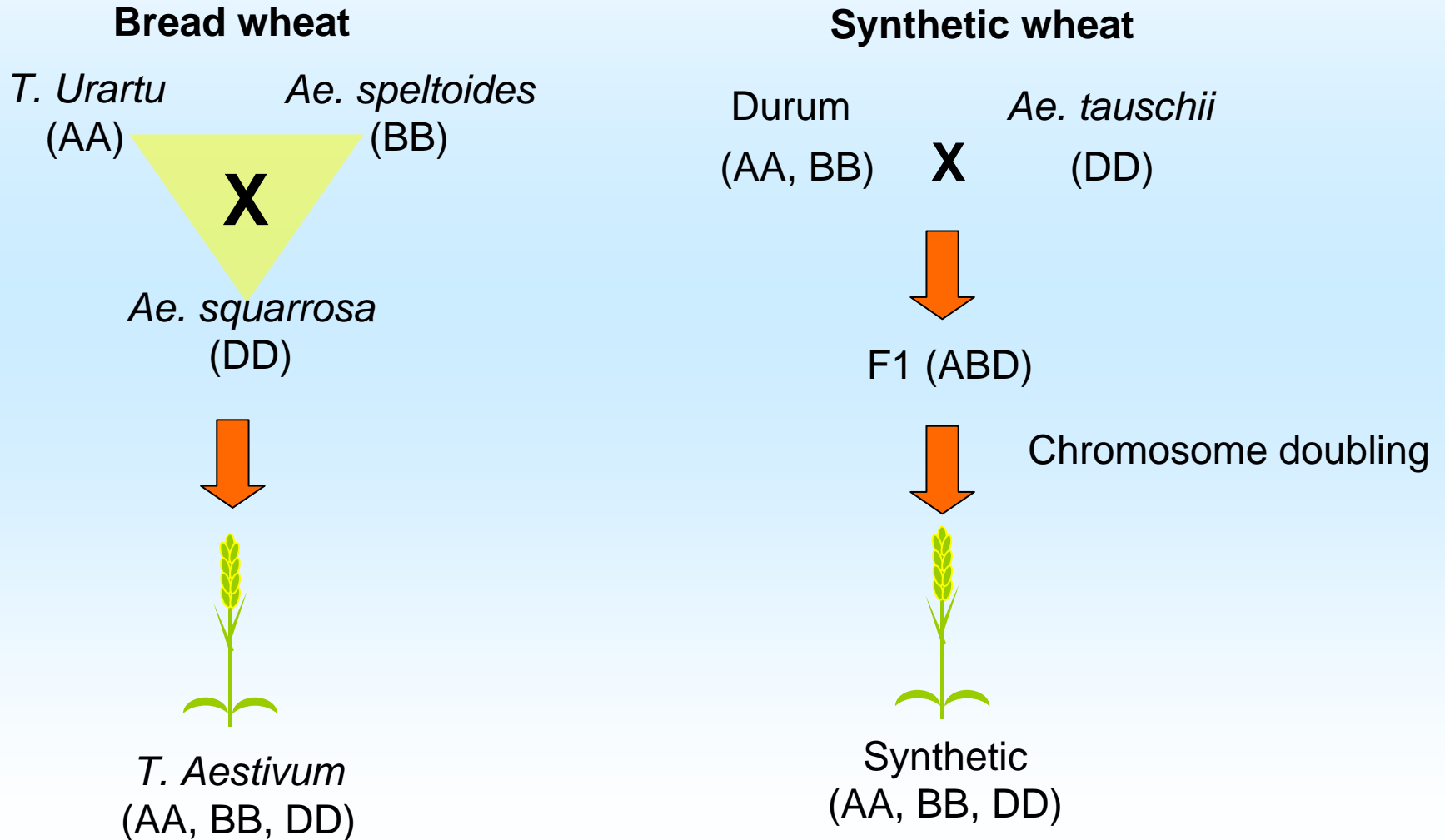
Sources of novel variation

- Synthetic hexaploid wheat (SHW)
- International germplasm – China, Russia
- Landrace, or traditional varieties
- Alien substitutions and translocations - 1RS-1BL, VPM
- Progenitor species – *Ae. tauschii*, *T. ventricosum*, *T. dicoccum*

Examples of the successful application of wide crossing to introduce alien genes into the hexaploid wheat genome at CIMMYT

Alien genes	Effect
1RS-1BL translocation from rye	Present in >300 cultivars
1RS-1BL translocation	Increased stress tolerance
<i>T. Taushii</i> x <i>T. turgidum</i>	Good yield characteristics
Synthetic hexaploids	Used in ~ 15% of CIMMYT bread wheat crosses
<i>LR19 (Ae. elongatum)</i>	Significant increase in yield and biomass

Synthetic wheat



Exploitation of SHW

- Development of UK adapted synthetic backcross derived lines (SBLs)
- Introgression of SHW alleles – test for selective advantage
- Development of SHW using winter-adapted durum as the tetraploid donor?

Conclusions

Identification and exploitation of natural variation is ongoing.

New methods are being developed which complement, but do not replace, the old.