

Genetical Genomics

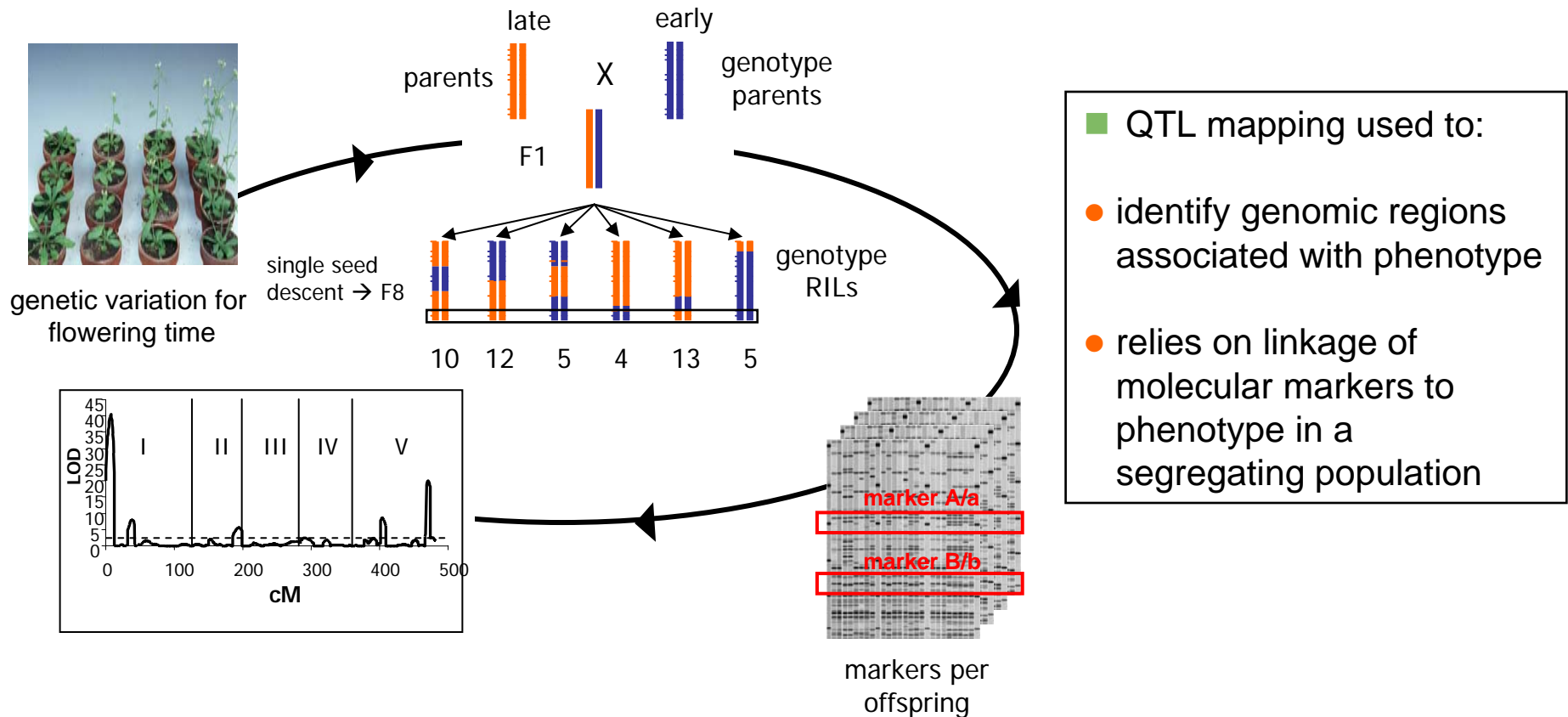
Linking QTL Mapping Studies With -Omics Technologies

Kim Boutilier

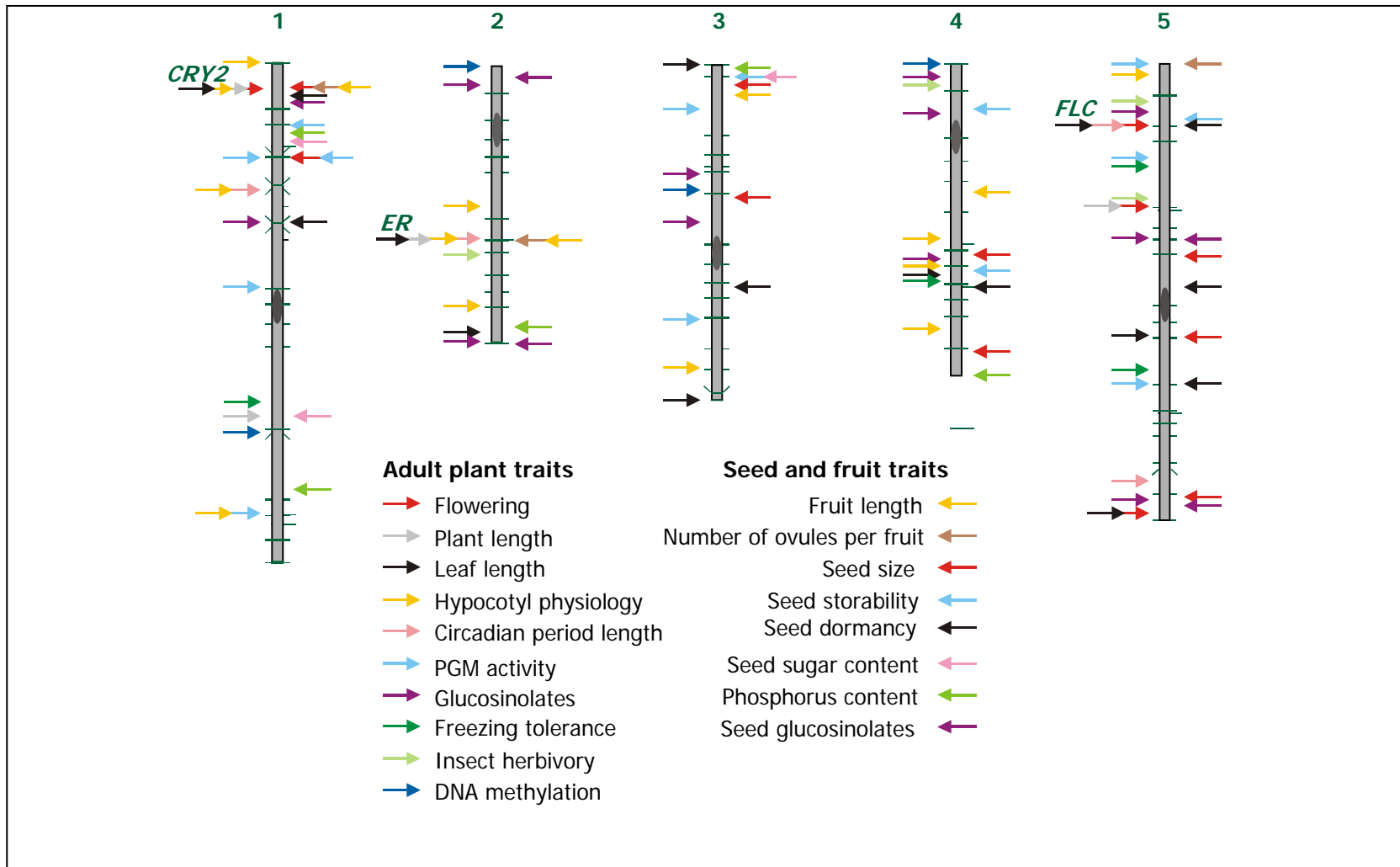


Quantitative Trait Locus (QTL) mapping

- agricultural traits often polygenic – phenotypes measured quantitatively
- loci controlling these traits are termed QTL



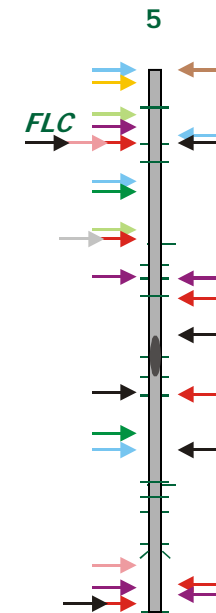
QTL mapped in Arabidopsis Ler-Cvi RIL population



From: Koornneef et al. Ann Rev Plant Biol 2004

Limitations of QTL mapping

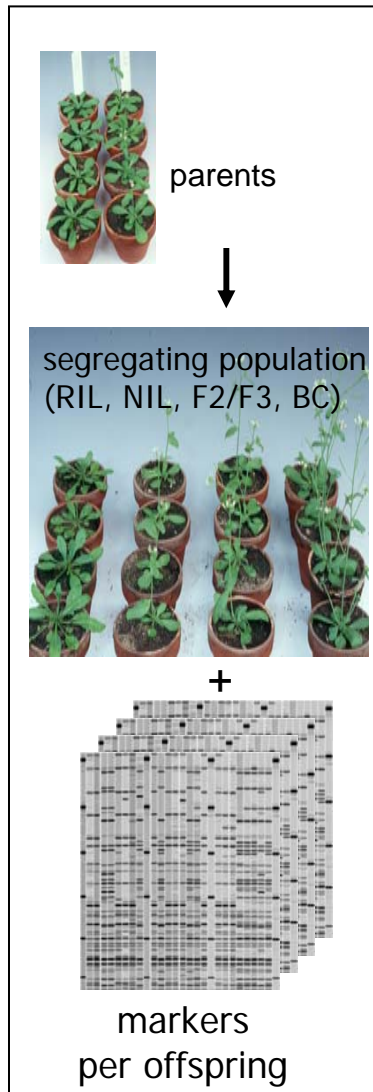
- Fine mapping within the QTL can reduce the number of candidate genes
- Even after fine mapping may be left with more candidates than can feasibly be pursued
- Need for an extra experimental step to bridge the gap between fine mapping and validation studies



Genetical genomics: the added value from segregation

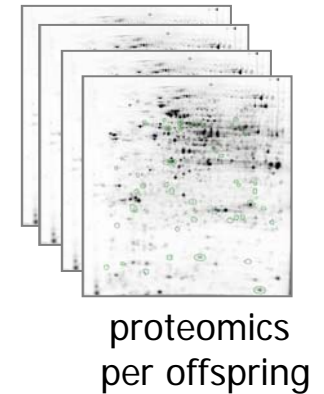
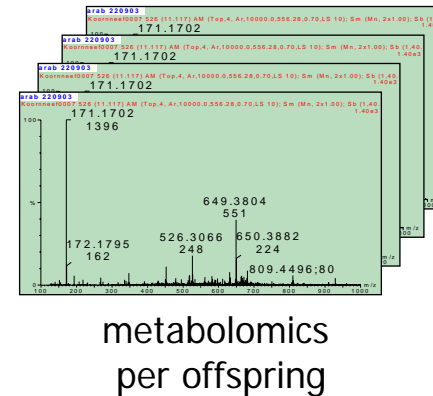
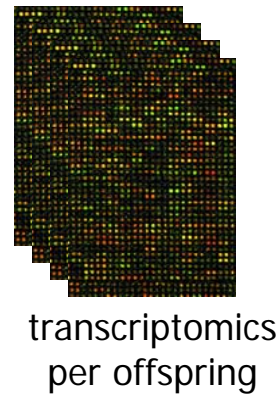
Ritsert C. Jansen and Jan-Peter Nap

Genetical genomics



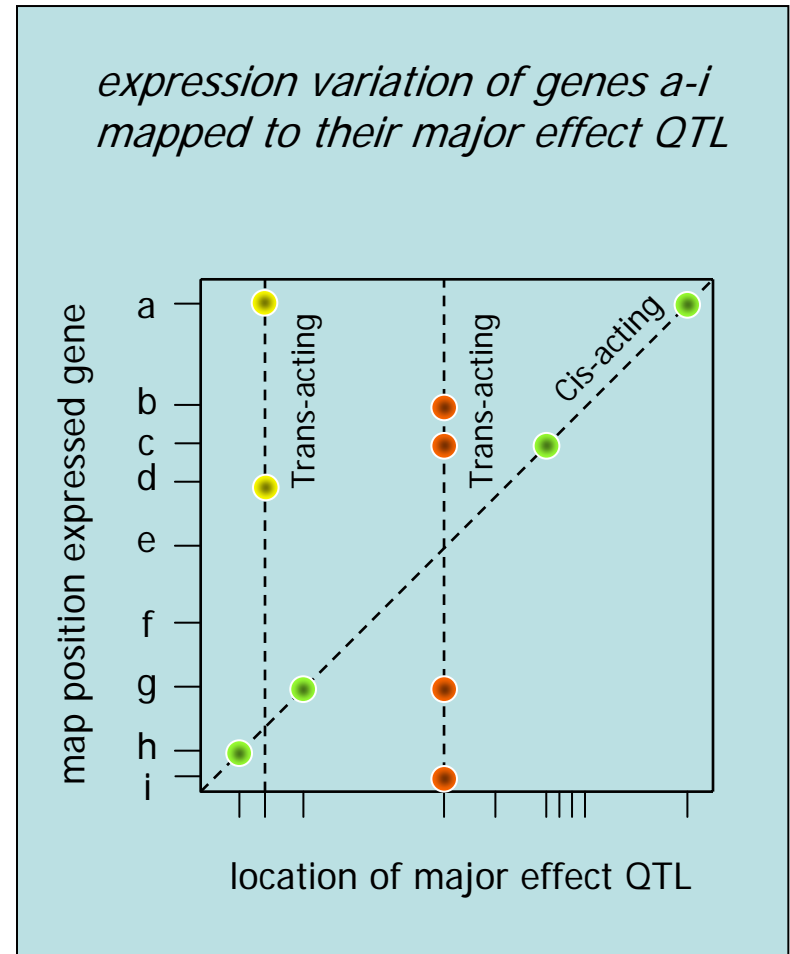
- combines expression profiling of individuals in a segregating population with molecular mapping
- expression level of each gene/protein/metabolite is treated as a QTL (eQTL)
- more powerful than either approach alone

+



Expected outcomes and utility for breeding

- Expressed genes regulated by *cis*-acting QTL
 - QTL maps to gene position
 - largest class
 - promoter/gene variants
 - candidate gene → target for MAS, genetic modification
- Few genes regulated by a single *trans*-acting QTL
 - QTL position different than gene position
 - QTL mapping to find markers for MAS on the *trans*-acting factor
 - candidate gene → genetic modification
- Groups of genes regulated by a single *trans*-acting QTL
 - master control genes
 - not useful for MAS due to potential unwanted traits
 - candidate gene → genetic modification

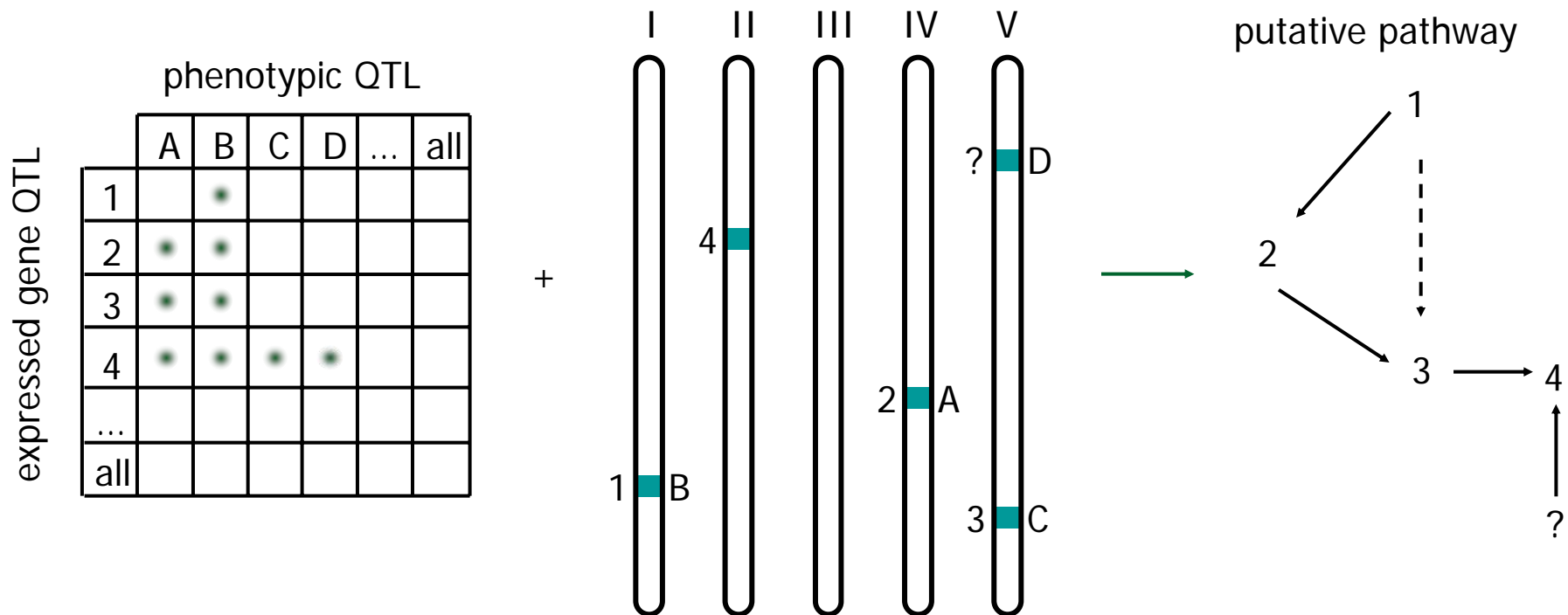


Pathway reconstruction

■ Combine:

- position on the genetic map of each QTL
- position on the chromosomes of each associated expressed gene (eQTL)

→ determine which genes influence the expression of other genes and in what order this influence is exerted.



Examples

- Most applicable to species with:
 - sequenced genome
 - segregating populations
 - good molecular marker maps
 - full (expressed) genome arrays

Trans-acting regulatory variation in *Saccharomyces cerevisiae* and the role of transcription factors

Gaël Yvert^{1,4}, Rachel B Brem¹, Jacqueline Whittle¹, Joshua M Akey¹, Eric Foss¹, Erin N Smith^{1,2}, Rachel Mackelprang^{1,3} & Leonid Kruglyak¹

NATURE GENETICS VOLUME 35 | NUMBER 1 | SEPTEMBER 2003

Genetics of gene expression surveyed in maize, mouse and man

Eric E. Schadt^{*†}, Stephanie A. Monks^{*†‡}, Thomas A. Drake[§], Aldons J. Luskis^{||}, Nam Che^{||}, Veronica Colinao^{||}, Thomas G. Ruff[¶], Stephen B. Milligan^{*}, John R. Lamb^{*}, Guy Cavet^{*}, Peter S. Linsley^{*}, Mao Mao^{*}, Roland B. Stoughton^{*} & Stephen H. Friend^{*#}

NATURE | VOL 422 | 20 MARCH 2003 | www.nature.com/nature

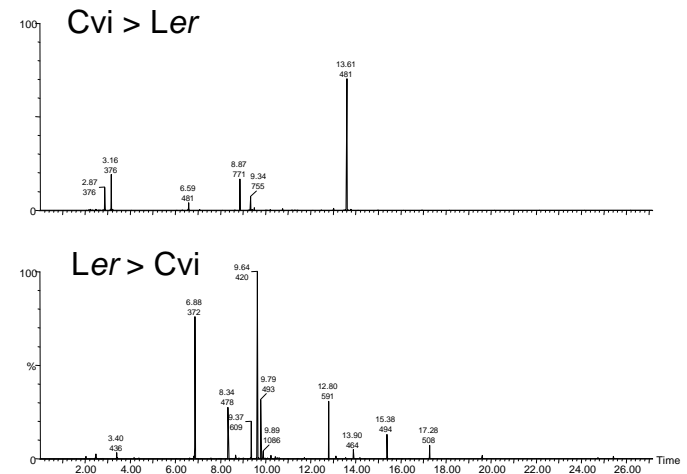
Genetic Dissection of Transcriptional Regulation in Budding Yeast

Rachel B. Brem,^{*} Gaël Yvert,^{*} Rebecca Clinton, Leonid Kruglyak[†]

26 APRIL 2002 VOL 296 SCIENCE

QTL Express – Maarten Koorneef WU

- Arabidopsis ecotypes (12) and RILs (162)
- QTL analyses on
 - GC-MS data
 - gene expression data
- Integrate data sets
 - co-location of QTL (RILs)
 - correlation of diverse data
 - physiological traits
 - metabolite content
 - gene expression
- Identify candidate genes
- Build regulatory network



Crucifer Nutrigenomics: Wageningen *Brassica* consortium

