



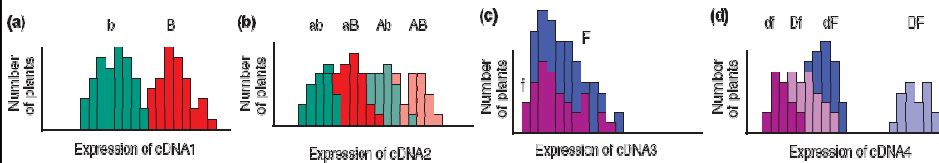
# Final Remarks

## Genetical Genomics & Systems Biology



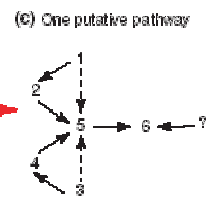
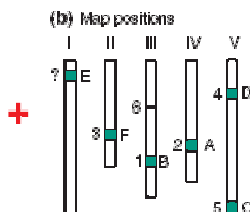
### Genetical Genomics

Use arrays to identify genes that are DE in relevant tissues of individuals sorted by QTL genotype. If those DE genes map the chromosome region of interest, they would become very strong candidates for QTL.



(a)

cDNA	Marker							
	A	B	C	D	E	F	...	all
1		*						
2	*	*						
3								
4				*	*	*	*	
5	*	*	*	*	*	*	*	
6	*	*	*	*	*	*	*	
...								
all								



TRENDS in Genetics

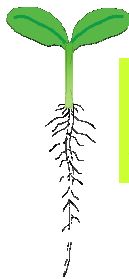
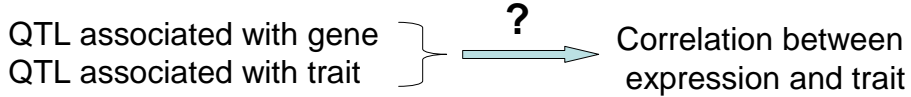
Source: Jansen and Nap, 2001



### Genetical Genomics

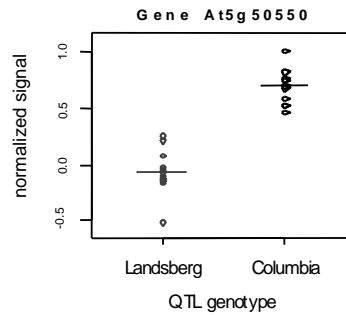
eQTL = expression QTL

If a gene's expression is found to link to the classical QTL, does the expression correlate with the shoot count trait?



**Goal: Find genome locations associated with gene expression**

DeCook et al. (2006)  
Genetics 172:1155-1164



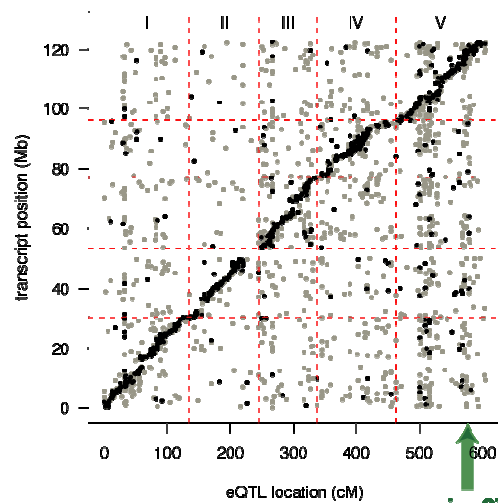
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### Genetical Genomics

eQTL = expression QTL

Controlled gene



- 2.5% FDR
- 10.0% FDR

Notice the **dark diagonal**. Most significant connections are often to itself.

DeCook et al. (2006)  
Genetics 172:1155-1164

Controlling position

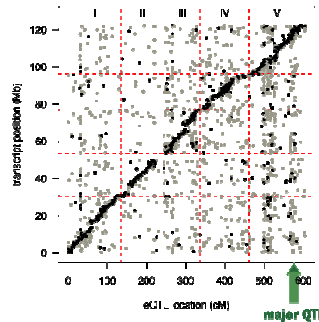
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Genetical Genomics

eQTL = expression QTL

- eQTL linkages
  - Cis-chromosomal effects (on diagonal)
  - Trans-chromosomal effects (off-diagonal)
- Vertical lines
  - Locations controlling many genes (Hot Spots)
  - Co-regulated genes?



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Genetical Genomics

eQTL = expression QTL

Assessing Significance

- Empirical Bayes hierarchical Mixture Over Markers (MOM):
- Shares information across both markers and genes
  - Get posterior probability that a gene maps nowhere,  $p_0$ ,  
and that the gene maps to marker  $m$ ,  $p_m$ , where  $\sum_{i=0}^M p_i = 1$ .
  - Threshold for significance, based on this posterior probability, chosen to coincide with a posterior expected FDR

Kendziorski, C.M., Chen, M., Yuan, M., Lan, H., and Attie, A.D. (2006) Statistical methods for expression Quantitative Trait Loci (eQTL). *Biometrics* 62:19-27.

Livestock

- C. Haley and D.J. de Koning (2006) Genetical genomics in livestock: potentials and pitfalls. *Animal Genetics* 37 (suppl.1):10-12.
- H.N. Kadarmideen, P. von Rohr and L.L.G. Jans (2006) From genetical genomics to systems genetics: potential applications in quantitative genomics and animal breeding. *Mammalian Genome* 17:548.

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### Genetical Genomics

Use arrays to identify genes that are DE in relevant tissues of individuals sorted by QTL genotype. If those DE genes map the chromosome region of interest, they would become very strong candidates for QTL.

Never enough! ...not greed but algebra:

.....particularly useful for:

$$V_q = 2pq\alpha^2$$

$$\alpha = a + d(q - p)$$

1. Speed up and enhance power to finding **New QTL**
2. Developing “**Diagnostic Kits**”
3. Deciphering the genetics of **Complex Traits**

A trait that is affected by many, often interacting, environmental and genetic factors such that no factor is completely sufficient nor are all factors necessary. (Andersson and Georges, 2004)

Ability to score individuals rapidly (and cheaply) at a very large number of loci.



### Genetical Genomics

Where does this leave **Quantitative Geneticists**?  
Where does this leave **Phenotypes** (the need to measure)?

Very well, .....I'm afraid (can't retire yet ☹)

#### Quantitative Geneticists:

- Never enough QTL
- Association studies
- Study of variation
- The individual needs to exist in order to be genotyped. With BLUP a prediction of a non-existent individual can be given

#### Phenotypes:

- Mutation is continuously generating new variation
- Selective breeding on genotypes reduces effective population size
- **Systems Biology:** Integration of all types of data



Final Remarks

Systems Biology

PNAS, Nov 2005, 102:17296

A data integration methodology for systems biology

Daehee Hwang\*, Alistair G. Rust\*, Stephen Ramsey\*, Jennifer J. Smith\*, Deena M. Leslie\*, Andrea D. Weston\*\*, Pedro de Atauri\*, John D. Aitchison\*, Leroy Hood\*\*‡, Andrew F. Siegel§, and Hamid Bolouri\*‡

\*Institute for Systems Biology, 1441 North 34th Street, Seattle, WA 98103; and †Departments of Management Science, Finance, and Statistics, University of Washington, Seattle WA 98195

My Own Interpretation

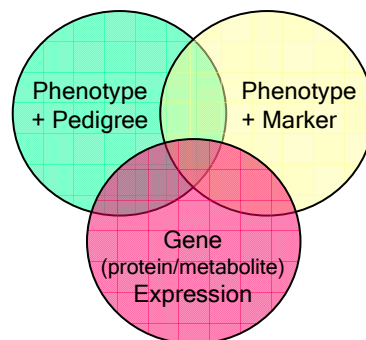
Systems Biology is about integrating data from different sources to provide a more comprehensive answer to a given biological question



Systems Biology

Predict Future Performance

3 Types of Data

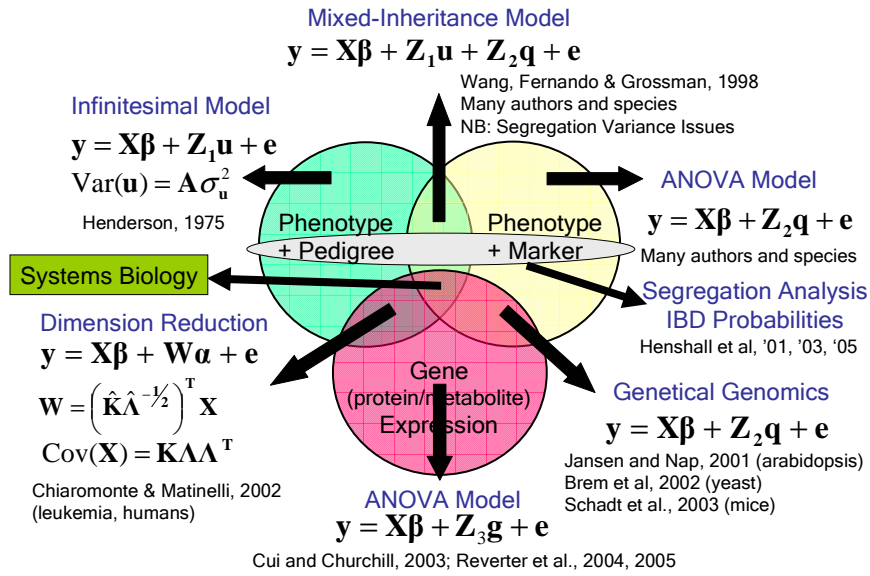


How to integrate them?



### Systems Biology

#### Predict Future Performance



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