BIOL2007 – QUANTITATIVE GENETICS: ADVANCED TOPICS

Summary
Topic 1: Phenotypic plasticity
Quantitative traits are expressed differently in different environments. If genotypes differ in level or direction of plasticity expressed, genotype-by-environment interaction exists.
Topic 2: Mapping quantitative genes
Use of molecular analyses to find locations of genes contributing to genetic variation in quantitative traits

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QUANTITATIVE TRAITS & MULTIPLE ENVIRONMENTS

Phenotypic plasticity (PP) = when same genotype produces different phenotypes in different environments. How to analyse this?
Reaction norms are a useful way to visualise a complex situation. These depict the phenotypes produced by different genotypes within a population in 2 or more environments. See Figure 5.1 (handout). This group of hypothetical reaction norms aid understanding of phenotypic plasticity and **genotype-by-environment interaction** ("**G by E"**).

Figure 5.1 shows the key elements of reaction norms for a case of two different environments: **X-axis** = environments, **Y-axis** = mean phenotypic values for each genotype. Each solid line connects the genotypic values in one environment to those in the other environment.

The key to the experimental approach is that these genotypic values are typically obtained for a "**half-sib breeding design**". In a half-sib breeding design, the data that is analysed comes from measurements on members of pairs of families. The pairs have one parent (father) in common. So the progeny have a known average degree of relatedness and this can be exploited to study **PP**.

Family members are reared in each environment. So slope of each line for each family is an estimate of the amount of plasticity for that family.

If the pattern of data for a population resembles that seen in **Figure 5.1A**: where the families are displayed as a series of parallel lines", then the population has **no plasticity**. The phenotypic mean of each family is same in each environment. There is **variance between families** – a spread of genetic values within environments – the amount of this variance is similar across the 2 environments.

If a population resembles **Figure 5.1B** with steep gradients of lines joining means in the pair of environments, then it indicates **high amount of plasticity**. The phenotypic means are very different between environments.

> Still see genetic variance (**between families**) within each environment.
> *Also - all families respond to 2 environments in exactly same way, decreasing by same amount (**slopes are parallel**) – so there is **no genetic variation in plasticity**

If a population resembles **Figure 5.1C** – Now there are large differences among families in plasticity (different slopes of reaction norms). Note that lines cross (no longer parallel), so the phenotypic rank of the families is different in the 2 environments. The families respond differently to the environments. This is called genotype-by-environment interaction (G x E).

Fig. 5.1D – here the reaction norms rarely cross. High variance in environment 2 and low variance in environment 1.

> Many individuals = plastic ("sloped" not "flat" reaction norms). However an approximately equal number of families increase and decrease their phenotypic values – hence means across all families don't differ between environments.

It is appropriate to analyse reaction norms via two-way ANOVA where the 2 main factors are genotype (sire/family) and environment. Individuals at each level of each factor are represented at each level of the other factor. Thus there are members of each half-sib family in each of the 2 environments.

To summarise the various outcomes:

Significant sire/family effect (Genotype, G) observed – this is evidence for overall additive genetic variance for the trait.

Significant environment (E) effect observed – this is evidence for overall plasticity.

Significant G-by-E interaction observed – this is evidence for additive variance for plasticity.

Illustrative example of G*E interaction:

Mazer & Schick (1991) – grew wild radish plants at 3 different densities (environments). Results for one trait, petal area are shown in "Figure 5.2".

Note the extensive crossing of the reaction norms. The sire-by-density (G*E) interaction is significant. Here the effect of sire (G) is also significant.

So if there was selection on petal area or on plasticity in petal area, then either or both could respond (evolve).

MAPPING QUANTITATIVE GENES

Much of the analysis of quantitative traits uses statistical techniques to make **indirect** assessments. Genome = a "black box". Difficult to answer questions about e.g. location of underlying genes, mode of action of these genes, how individual loci vary in their effect size. Recent progress has been made bycombining molecular genetics + theoretical + statistical innovations allows **"quantitative trait loci (QTL) mapping"**. This locates regions containing genes affecting quantitative traits and constitutes the first step toward functional knowledge of quantitative genes.

STEP 1 – create a genetic map, preferably of whole genome. Ideally have many DNA-based markers evenly and closely spaced throughout genome. To make a map, usually make a **mapping population** by crossing together genetically divergent populations (e.g. inbred lines).

> Cross one individual from population1 to one individual from population 2 to create an F1. The F1 is highly heterozygous (because divergent parental populations fixed for different alleles at different loci). Also it has high linkage disequilibrium (because chromosomes from parental populations haven't had opportunity to recombine).

STEP 2 – make an **F2 mapping population**. Either self-fertilise an F1 individual or mate a pair of F1 individuals together or mate an F1 individual mated to an individual from one of the parental populations ("backcross").

> Recombination produces unique combinations of genomes from the parental populations in each F2 individual. Frequency of recombination between markers from parents used to construct the map because frequency of crossing over between markers increases with increasing distance apart on chromosome. Map distance between 2 markers denoted in centimorgans (cM) where 1 cM denotes recombination rate of 1%.
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> See **FIGURE 5.17 (on handout)** - shows recombination among **3 linked marker loci** in an F2 mapping population. Most of F2 = parental (n = 4) or F1 (n = 3) genotypes. The frequency of the others (n = 3 recombinants) – allows estimation of the distance between loci. Individuals **8** & **9** = recombination between **A** & **B** loci. Individual **10** = recombination between **B** & **C** loci. If proportions true of larger sample of F2 progeny then recombination fraction ***r***, = 0.1 for A & B (2/20) & A/B ~ 20 cM apart: ***r*** = 0.05 for B & C (1/20) & B/C ~ 10cM apart

STEP 3 - generate a genetic map showing markers in linkage groups – see **Figure 5.18 (handout)** for 2 monkey flower species.

STEP 4 – test for association between variability in DNA markers and variation in the phenotypic trait. If certain marker bands occur with certain values of the trait more often than expected by chance, then this is evidence that a QTL affecting this trait is linked to the marker. So need new statistical tests to test for potential associations. For example, **log-odds ratio** or **LOD score:**

> **LOD = $\log_{10}$ (L_1/L_0)** where L_1 is likelihood that there is a QTL linked to a particular marker, given the data & L_0 is probability of no QTL near that marker.
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> Results shown as LOD plots for a given linkage group (see **Figure 5.20 on handout**). Each horizontal line denotes a **statistical threshold**. Above that line = significant for a QTL at that location. Below that line = spurious association due to chance.

An association between **Vp** and a **marker** = evidence that a locus that affects trait (a **QTL**) is linked to that **marker**. So, finally, **STEP 5** - place QTLs onto genetic map (**Figure 5.21 - handout**).

> Position given with a confidence interval for floral differences in cross between a habitual selfer and a habitual outcrosser. This example shows several loci identified with effects on flower traits (see Table on Handout). Effect of each locus is moderately strong (7.6% to 28.6%). Statistical support for each QTL generally increases with increasing effect of the locus on the phenotype.

*Note that a limitation of all current QTL studies is that they have **low resolution** because markers only occur every 10 cM or more and this distance can contain several hundred genes. Perhaps one should rename QTLs as Quantitative Trait Regions…

Ultimate goal is to identify and perform functional analysis of genes affecting the phenotype.

> For example, the *candidate gene approach*. If a known gene corresponds to same region as a QTL for a quantitative trait, it is a candidate gene for that trait.
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> **Example**: QTLs for lifespan in Drosophila co-map with genes involved in basic metabolism, breakdown of insulin, protein synthesis, response to stress. Intuitively makes sense but much more specific data needed in future…….