On the correlation between heterozygosity and fitness in natural populations
Background

• Inbreeding increases the level of homozygosity on a genome-wide basis
  – Depression of fitness as a result of the expression of partly recessive deleterious alleles and the loss of the heterozygote advantage

• Indirect estimates of inbreeding used to study fitness effects
  – Based on allelic data at molecular markers
Background

• Three primary hypotheses currently prevail for correlations between heterozygosity and fitness

• Relative importance of hypotheses remains unclear
  – Screening of heterozygosity at polymorphic DNA markers offers an opportunity to resolve the issue
Direct Effect Hypothesis

- Heterozygote advantage as a result of functional overdominance at the scored loci _per se_
  - Potentially important in allozyme studies
    - Biochemical system will be more efficient in heterozygotes than in homozygotes
  - Less important in studies using noncoding DNA markers such as microsatellites
Local Effect Hypothesis

• Apparent heterozygote advantage at the markers as a result of effects of homozygosity at closely linked fitness loci
  – Requires linkage disequilibria
    • Recently bottlenecked-and-expanded populations
    • Intermixing of genetically different populations
    • Genetic drift in small populations
    • Selection
General Effect Hypothesis

• Apparent heterozygote advantage at the markers as a result of effects of homozygosity at genome-wide distributed fitness loci
  – Requires identity disequilibria
    • Partial inbreeding
### Observed Multilocus Heterozygosity-Fitness Correlations

<table>
<thead>
<tr>
<th>Study species</th>
<th>Result</th>
<th>Main hypothesis</th>
<th>Alternative hypothesis</th>
<th>Excluded hypothesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rainbow trout <em>Oncorhynchus mykiss</em></td>
<td>Heterozygosity–condition correlation at allozymes but not at microsatellites (Thelen &amp; Allendorf 2001)</td>
<td><strong>Direct effect hypothesis</strong> because only one type of markers (allozymes) is informative</td>
<td>Local effect hypothesis because extended linkage disequilibrium is expected because of recent population bottleneck and expansion</td>
<td><strong>General effect hypothesis</strong> because a large number of highly polymorphic markers make a correlation with the inbreeding coefficient likely</td>
</tr>
<tr>
<td>Great reed warbler <em>Acrocephalus arundinaceus</em></td>
<td>Heterozygosity–survival association at microsatellites in full sibs (Hansson et al. 2001)</td>
<td><em>Local effect hypothesis</em> because allozymes might be located in particular gene-rich chromosome regions, and therefore be in linkage disequilibrium with fitness loci</td>
<td>Direct effect hypothesis because microsatellites might not be selectively neutral <strong>General effect hypothesis</strong> because there might be within-pedigree variation in level of homozygosity</td>
<td></td>
</tr>
<tr>
<td>Red deer <em>Cervus elaphus</em></td>
<td>Heterozygosity–birth weight correlation at a large number of microsatellites (Slate &amp; Pemberton 2002)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**General effect hypothesis** because extended linkage disequilibrium is expected as a result of recent population bottleneck and expansion.
Future Directions

• Few studies give conclusive evidence for either of the primary hypotheses to explain multilocus heterozygosity-fitness correlations
  – Pressing need to design future studies that would evaluate their relative importance in natural populations
  – Important to report null results to assess the generality of correlations in natural populations