

BIOS 317 - Evolution - Spring 2012

Lecture 11 (10 February)

What is the result of chromosome inversions? How does polyploidy contribute to genetic variation?

Exam 1, Friday, Feb. 17, 40 multiple choice questions, but in some cases there will be several questions on a single theme, often illustrated with graphs. Exam is 40 points (of 215 total). “Questions of the week” will provide a useful guide to the kinds of questions. “Learning objectives” at the start of each set of lecture notes provides a study guide.

Reading: F&H 1–3, 5 (chapter 4 will be covered later in the course, but note that some basic ideas in systematics are covered in chapters 1-3)

Material: With the caveats pointed out with the questions of the week, all was covered in lecture (lectures 1-11), but the reading can enhance your understanding of the lectures, particularly information in figures presented in lecture: science and the scientific method, Darwin, Darwin's theory, levels of selection, HIV and other examples of levels of selection, general tools and methods of evolutionary theory, where does variation come from....

Where variation comes from, continued:

Chromosome alterations

Chromosome inversions—(**Figure 5.9**) generally prevent crossing over because inversion heterozygotes cannot recombine normally and produce viable gametes. Leads to a group of alleles being inherited in a single pack. For a long time this was thought to be very important in evolution (**Figure 5.10**; recall the common notion in science of “looking where the light is”: during this time inversions were visible and could be analyzed, while gel electrophoresis of proteins or directly sequencing of genes were still impossible; older evolution texts had whole chapters on chromosome inversions, now it is barely mentioned...but still may have a role in preventing recombination).

polyploidy—genome duplication, typically duplication of entire sets or chromosomes. Can be relatively benign at level of organism despite greater amount of DNA. Will likely be selected for at the level of the gene and genome.... Common in many land plants, but rare in many or most animals, usually begins (**Figure 5.11**) with errors at meiosis that result in diploid gametes ($2n$); self-fertilization can lead to $4n$ individual which can again self-fertilize or mate with another $4n$ individual. More complex are situations when $2n$ gametes fertilize or are fertilized by $1n$ gametes; triploids which have homologous chromosomes in an odd number are problematic during meiosis; self-fertilization of a triploid however can often work, but usually a barrier to gene flow. Often polyploidy can create new species because of problematic $2n$ and $4n$ crosses.

New material (not on exam 1):

How much heritable variation is in natural populations?

To understand why this question was given so much attention in evolutionary biology, one has to consider the socio-political context of the early 20th century. This was the time when “progressive” movements flourished. Science and logic were going to make the world a better place (e.g., by banning alcohol). “Feeble-minded” people would be sterilized, thus eliminating deleterious alleles from the population that ordinarily would be removed by selection. Evolutionary biologists were leaders in the “progressive” movement of eugenics.

The actions of William Jennings Bryan can be best understood in this context. Often presented as unenlightened for his opposition to the teaching of evolution (p. 97-98), Bryan saw eugenics as a threat to the poor and unenfranchised (i.e., it was easy to decide that someone was feeble-minded if they were an immigrant who didn't speak much English). He invented the creationist movement as a political tool to counter eugenics, not because he literally believed in the Bible (he didn't). Opposition to the teaching of evolution even today has its roots in some very real problems with how evolutionary theory was applied!

Anyway, this was a question that long vexed evolutionary biologists; some argued that any variation is bad and would be removed rapidly by selection (“classical” view and the basis for eugenics); some argued that balancing selection would maintain variation that could be adaptive in a changing environment (“balance” view, in part politically and socially motivated as a counter-argument to eugenics, best illustrated by the simple 1-locus, 2-allele case of heterozygote superiority such as sickle cell anemia in malaria environment [AS>AA>SS]; selection on heterozygote maintains the diversity of alleles; also leads to the concept of “genetic load,” the load of deleterious alleles that a population carries). Often, but not always, scientists aligned themselves and their scientific views to their political leanings.

Some early evidence in this debate was the existence of chromosomal inversions. Here was heritable variation: was it under selection? How much of it was there in natural populations?

The real breakthrough was gel electrophoresis of proteins (**Figure 5.12**: note that this is still a phenotypic assay, though one that is directly related to genotype). Gel electrophoresis showed that populations are highly variable (**Figure 5.13**: heterozygosity is the fraction of genes that are heterozygous in the genotype of these diploid species). More modern techniques (sequencing) supports these results and shows that Single Nucleotide Polymorphisms, or SNPs, are very common, with perhaps millions of common variants in human populations. These very high levels of genetic diversity have led to a third interpretation—most of this variation is neutral with respect to organismal fitness (this was

a brilliant reconceptualization of the classical view). Note that the neutral theory does not assume that most mutations are neutral, only that some are, and it is these neutral mutations that accumulate in the genome. And a fourth interpretation is suggested by this course—conflicts between levels of selection, some variation may be selected against or neutral at level of organism, but selected for at level of gene. This can lead to genetic and genomic diversity, or sometimes to mechanisms to limit such diversity, such as RIPPING in *Neurospora* to counter any mobile genetic element (consequently a small genome). Balancing selection may be achieved by levels-of-selection conflicts. All four hypotheses are likely relevant to some aspects of genetic variation.

Genomics now makes it clear that most of the genome of eukaryotes is not even genes; we know very little about what genomic variation means or its significance. Comparative and evolutionary views can begin to illuminate this variation (**Table 5.1**)

As well, new selective challenges can arise that make neutral variation or near-neutral variation adaptive—example of evolution of HIV in humans; variation of RT enzyme active site was initially neutral (or even selected against), but in the presence of AZT certain of these variants were selected for, and selection molded these variants further.

Variation in the human CFTR (cystic fibrosis transmembrane conductance regulator) gene—exhibits how common genetic variation is (**Figure 5.14**). This is clearly not neutral variation, but as we'll see shortly, a recessive, loss-of-function allele can persist in a population at low frequency because it is only selected against in the homozygous condition. As shown by this example, a LOF “allele” can actually be many different alleles caused by different LOF mutations.... Now (Nature 9 Feb 2012) gene therapies have actually targeted particular mutations.

So that's where variation comes from, one of the two questions that so vexed Darwin, and there is clearly a lot of heritable variation in modern populations.