

POPULATION GENETICS

Winter 2005

Lecture 19

Speciation

- speciation is the process by which new species are formed from previously existing ones.
- in Darwin's words speciation is the "multiplication of species".
- species can thus be viewed to "reproduce" much like individual organisms.
- in fact, it is common to talk of a "parental" species giving rise to a "daughter" species (species are like ships in that we don't talk about "sons" being produced).
- although it is possible for us to draw a parallel between reproduction at the individual level and reproduction at the species level, there is an important difference between these processes.
- individual organisms have been "programmed" by their genetic systems to reproduce.
- there is no such selection acting at the species level.

- if we use the biological species concept, speciation occurs when populations acquire **reproductive isolating mechanisms**.
- these barriers may act to prevent fertilization – this is called **prezygotic isolation**.
- this typically involves changes in location or timing of breeding, or courtship displays.

- barriers may also occur if hybrids are inviable or sterile – this is **postzygotic isolation**.
- postzygotic barriers act after mating to prevent hybrids from backcrossing into either parental species.

Modes of Speciation

1. Allopatric speciation

- most widely accepted mode of speciation.
- has wide support from studies on geographic variation among species.
- championed by Ernst Mayr, although the allopatric model of speciation is clearly the one that was favored by Darwin as well.

- the first step in the process is the geographic separation of two populations of the same species.
- the isolation of the two populations has an immediate and important consequence:
it eliminates the movement of genes between the two populations.
- no gene flow allows the two populations to begin to evolve independently of one another.

- under the classic allopatric model the barrier that once separated the two populations is eventually removed and the populations establish what is called "secondary contact".
- what happens next is discussed in a later section.

Parapatric speciation

- parapatric speciation is similar to allopatric speciation but the two populations do not become completely separated but remain connected over a narrow contact zone.

- the two populations begin to diverge genetically while continuing to exchange migrants across a small zone of contact.
- commonly a hybrid zone is established.
- the width of the hybrid zone depends on the mean dispersal distance of the species involved and the strength of selection.
- to produce a new species under the parapatric model, the strength of selection acting in the two environments must be strong and the dispersal capabilities generally limited.
- in this regard, the parapatric model differs from the allopatric model.
- what is the evidence for parapatric speciation?
- evidence for parapatric speciation comes mainly from the existence of **ring species**.
- a ring species is a connected ring of species.
- for adjacent species that contact one another in their range, hybridization occurs.
- for species situated further apart in the ring, the ability to interbreed is diminished.
- for species located at the ends of these interconnected populations, reproductive isolation is complete.
- a particularly interesting example of ring species in California involves salamanders of the genus *Ensatina*.
- species of *Ensatina* diverge from the northern part of California and fold around either side of the central valley.
- interbreeding occurs between species that make contact with each other on both sides of the valley.
- when the two terminal species make contact at the southern end of the central valley, no interbreeding occurs - isolation is complete.

Sympatric speciation

- sympatric speciation occurs when reproductive isolation is formed between two groups of a population while they remain sympatric.
- recall that under the allopatric model the genetic divergence that occurs over time between the geographically isolated populations is slow and gradual.
- many loci may be involved and the strength of selection required to drive this divergence can be small (because gene flow has ceased between populations).
- under the parapatric model, the strength of selection must be greater to maintain the differences between the populations because of the fact that they remain in contact and continue to exchange small number of migrants each generation.
- under the sympatric model, the conditions become even more restrictive for speciation.
- the reason for this is that it is likely that individuals of the two diverging groups to come into contact and reproduce.
- when they do, the genetic differences developing between the groups would be eliminated.
- most models of sympatric speciation are highly controversial.
- from the time of the modern synthesis up until very recently, the importance of sympatric speciation was greatly downplayed.
- most models of sympatric speciation require that at least two genetic loci be involved.

- in the example outlined in the textbook involving *Rhagoletis* fruit flies, one of these genes is involved in host (i.e., fruit) recognition, the other for larval survivorship once the egg is deposited in the host.

What are evolutionary processes cause speciation?

1. Natural selection

- this is by far the most important evolutionary process causing speciation.
- driven by different abiotic conditions (e.g., temperature, altitude) and biotic conditions (e.g., competitors, parasites).
- under the classic allopatric model, speciation results as an **incidental by-product** of the action of natural selection acting in different populations over evolutionary time scales.
- there is no direct selection for speciation – this is simply a secondary consequence of independent evolution.

2. Sexual selection

- Darwin recognized that species-rich groups tended to those in which strong sexual selection may be occurring.
- this matter is only recently being given the attention it deserves.
- recently, studies have suggested that sexually antagonistic genes and speciation may play an important role in speciation.
- in examining the source of reproductive isolation, we can broadly define two classes of genes: those that cause sterility in hybrids and those that cause hybrids to be inviolate.
- recent work in *Drosophila* has suggested that genes causing sterility in hybrids evolve at much faster rates than those that affect viability.
- in fact, about 10X more genes appear to cause sterility than viability.
- when we look at the proportion of genes that affect sterility and viability within species, exactly the opposite pattern is seen - genes that affect viability are 10X more common than those that cause sterility.
- what is the explanation for this?
- we don't really know but it could be a consequence of sexually antagonistic genes - those that benefit males at a cost to females and vice versa.
- the rapid and continuous evolution of these loci could be a major “engine of speciation”

3. Random genetic drift

- may involve founder effects and genetic bottlenecks.
- not important in either parapatric or sympatric speciation but may play some (minor) role in allopatric speciation.
- here, neutral mutations may accumulate in different geographically separated populations that may not be neutral in hybrids.

What causes post-zygotic isolation?

- after many years of study, we can make some generalities about the evolution of reproductive isolation.
- first, the magnitude of both pre-zygotic and post-zygotic isolation increases with the time since the splitting of the populations.
- the time required for full reproductive isolation is variable among different groups.
- in *Drosophila*, it takes about 1.5 to 3 million years for this to occur.
- in other groups (such as African cichlids) it can occur much more quickly.
- in marine bivalves, it may take 7 or 8 million years!
- second, among recently separated groups pre-zygotic isolation is generally a stronger barrier to gene exchange than post-zygotic isolation.
- third, in the early stages of speciation, hybrid sterility or inviability is almost always seen in males (in taxa where males are the heterogametic sex).
- in the case of *D. simulans* and *D. mauritiana*, hybrids are completely viable yet males are completely sterile!
- this shows that post-zygotic isolation evolves more quickly in males and is called **Haldane's rule** after J.B.S. Haldane.
- despite these generalities, we know very little about the genetic basis of reproductive isolation.
- however, we are finally making progress in understanding the genes responsible for causing reproductive isolation!
- the underlying mechanism thought to cause post-zygotic isolation is through **Dobzhansky-Muller incompatibility**.
- both Dobzhansky and Muller thought that epistatic interactions between loci were responsible for the reduced viability and fertility of hybrids.
- for example, suppose an ancestral $A_1A_1B_1B_1$ population gave rise to an $A_2A_2B_1B_1$ population and an $A_1A_1B_2B_2$ population.
- if hybrids are formed, they are either inviable and/or sterile because they possess A_2 and B_2 alleles that are incompatible with one another.
- the numbers of genes that underlie post-zygotic isolation may be small at the early stages of divergence but such incompatibilities will accumulate through time.

Important questions:

- 1. What kinds of genes contribute to reproductive isolation?**
- 2. What are the normal functions of these genes?**
- 3. How did these normal functions diverge among populations ultimately leading to reproductive isolation?**

- recently, detailed studies have been done on several "speciation genes"
- Wu (2004) defines a speciation gene as a gene that can be shown to cause some degree of ecological, sexual, or post-zygotic isolation between recently separated (or nascent) species.
- most genes that have been identified exert large effects on fitness – this may not be typical since there is a strong bias against detecting genes of weaker effect.

What types of genes are involved in speciation?

- here are some recent examples.

1. The *Xmrk-2* gene in *Xiphophorus* spp.

- many species of *Xiphophorus* fishes have spots on composed of black pigment.
- in crosses between *X. maculatus* (platys) and *X. helleri* (swordtails) these spots occasionally develop into malignant melanomas.
- there are thought to be two genes involved in causing melanomas – one of these has been identified as an X-linked gene called *Xmrk-2* that encodes for a transmembrane growth factor receptor.
- its closest homologue in humans is the epidermal growth factor receptor (EGFR) locus.
- the *Xmrk-2* gene only causes tumors when this second locus is absent.
- mutations at *Xmrk-2* can stop the formation of tumors.
- if the gene is upregulated, the incidence of tumors increases.
- this gene arose from a duplication of the *Xmrk-1* locus.

2. The *OdsH* gene in *Drosophila*

- this example was published Ting et al. 1998, Nature 282: 1501.
- it involves a gene responsible for postzygotic isolation between two *Drosophila* species: *D. simulans* and *D. mauritiana* (found on Mauritius).
- hybrid males of *D. simulans* x *D. mauritiana* are sterile.
- this is an example of **Haldane's rule** in which the sterile sex is “heterogametic” (i.e., has two sex chromosomes).
- here, male *Drosophila* are XY, females are XX.
- the “sterility factor” in the *D. simulans* x *D. mauritiana* hybrids was traced to small region of X chromosome.
- in this region a gene was identified that codes for a transcription factor possessing a 180 bp homeobox.
- this identifies the gene as a **homeotic gene** since the homeobox (representing a DNA-binding domain) is a defining feature of the former.
- *OdsH* is only active in male testis (in spermiogenesis?) and is experiencing strong positive selection.
- in fact, more amino acid changes were identified in the homeobox in the past 500,000 years (representing when *D. mauritiana* diverged from *D. simulans*) than the preceding 700 million years!
- the effect of the *OdsH* gene is surprisingly small in *D. melanogaster*.
- if the gene is deleted, males suffer a 40% reduction in fertility when they are two days old and are forced to mate repeatedly.
- over the next two days of age, the reduction in fertility vanishes.
- this suggests that function of the *OdsH* gene is to accelerate the maturation of sperm.

3. The *Nup96* gene in *D. melanogaster*

- this gene was isolated from *D. melanogaster* by complementation mapping by Presgraves et al. (2003).
- unlike the *OdsH* gene, the *Nup96* locus causes hybrid inviability.
- this gene encodes a subunit of a nucleoporin protein, one of about 30 proteins that constitute the nuclear pore complexes that regulate the passage of proteins and RNA between the nucleus and the cytoplasm.
- this protein has also been found to have experienced strong positive selection in the early stage of divergence between *D. melanogaster* and *D. simulans*.
- the *Nup96* gene interacts with at least one other locus to produce Dobzhansky-Muller incompatibility that has been mapped to the X chromosome.
- it is unclear if there are other X-linked genes that interact with *Nup96*.
- the rapid divergence at the *Nup96* gene is surprising because nucleoporin genes are typically highly constrained.
- however, these results show that divergence at a normal “housekeeping” gene can cause hybrid inviability.

4. *desat-2* in *D. melanogaster*

- *D. melanogaster* has radiated out of Africa with humans currently lives all over the globe (in our garbage cans).
- female flies from Africa possess a different cuticular hydrocarbon than found on adult females throughout the rest of the world.
- the difference is due to a different position of a single double bond in a long chain of saturated hydrocarbons.
- this difference is due to the loss of function of the *desat-2* gene in cosmopolitan populations.
- why would the loss of this gene be beneficial to flies not living in Africa?
- when the *desat-2* gene is knocked-out in African flies, the result is an increased tolerance of cold and a decrease in starvation tolerance.
- therefore, the loss of this gene may have been adaptive as *D. melanogaster* radiated into cooler climates.
- there is an interesting pleiotropic effect of this *desat-2* mutation that involves mate choice.
- when African females are placed with African (A) and Cosmopolitan (C) males, they only mate with the former.
- the presence of this modified hydrocarbon on the cuticle of the female affects her smell – in effect they wear a different perfume.
- apparently, they are not courted very intensely by C males.
- this gene is thus acting in two different ways – one to allow adaptation to cooler climates and secondarily through mate choice.

5. The *Hmr* (hybrid male rescue) gene in *Drosophila*

- *D. melanogaster* and *D. simulans* speciated about 2.5 MYA.
- male hybrids between these species are both inviable and sterile.

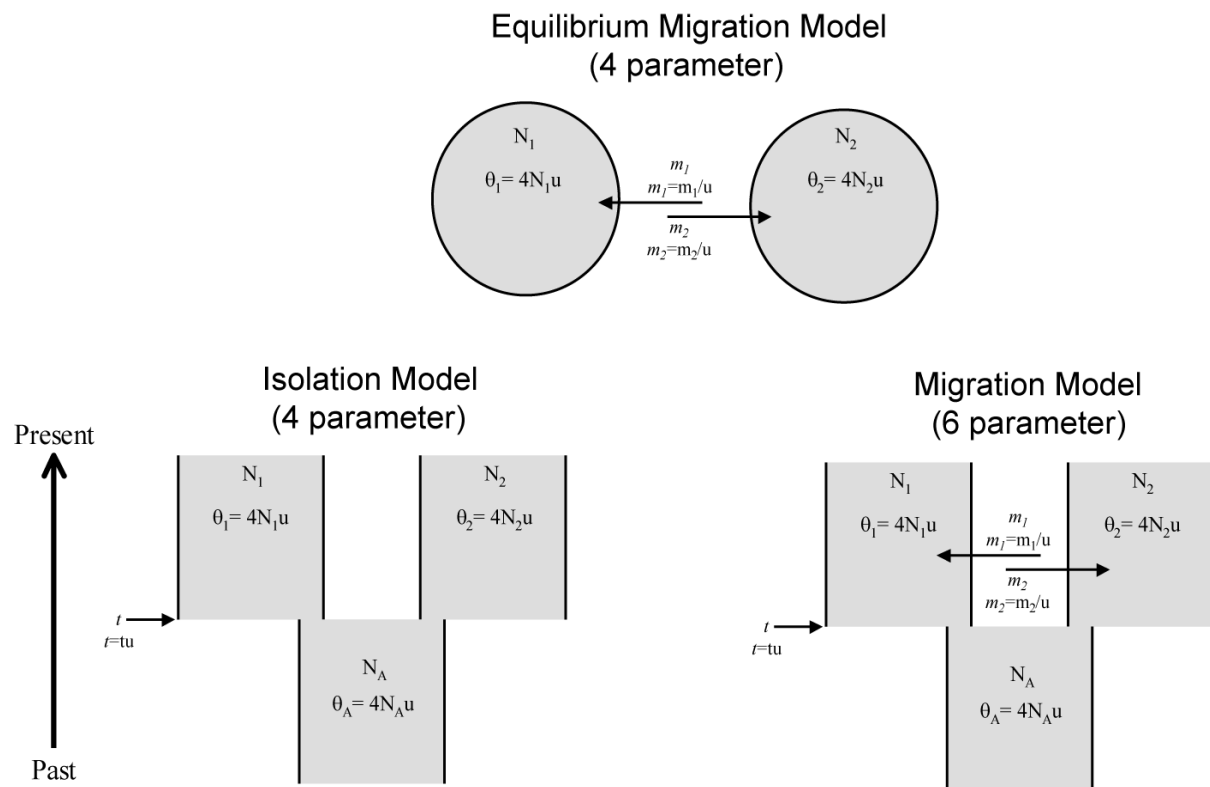
- five mutations that “rescue” the inviability of hybrids have been discovered.
- one of these is the *Hmr* gene located on the X chromosome that encodes for a transcription factor.
- there are two DNA binding motifs in the gene and these regions have experienced many amino acid substitutions between the two species.
- this suggests the action of positive selection.
- however, the mutation actually responsible for rescuing viability was a P-element insertion in the 5’ region of the gene that caused a large reduction in transcription.

What do these limited examples tell us about speciation genes?

- not surprisingly, there is a wide range of genes that are capable of causing reproductive isolation to evolve.
- at the *Xmrk-2*, *OdsH*, *Hmr*, and *desat-2* loci, changes in the transcriptional regulation of the gene have played crucial roles in causing sterility or inviability.
- this supports an old hypothesis that regulatory evolution is more important than in evolution than structural evolution.
- however, the divergence of the *Nup96* gene suggests that other avenues are possible too – although even in this case it is still not possible to exclude the contributing role of regulatory changes (since these have not yet been studied).
- there is also a clear trend for speciation genes to be sex-linked.
- why would this be?

Testing modes of speciation

- although the allopatric mode of speciation is widely accepted by most biologists, there is actually little direct genetic support for over other models such as parapatric speciation.
- the allopatric model assumes complete geographic separation with no gene flow.
- the parapatric model assumes the populations are not completely isolated but continue to exchange genes while natural selection operates to adapt the populations to different conditions.
- do most species originate in the absence of gene flow?
- or, do they evolve to become independent lineages while continuing to exchange genes at a low level?
- we are now in a position to test this possibility using a method developed by Neilsen, Wakeley, and Hey.
- the approach is to use a coalescent model to test for complete isolation (the allopatric null hypothesis), or isolation with migration (the parapatric alternative hypothesis).



- the power of this approach is based on the incorporation of data from multiple gene genealogies.
- if the isolation model is correct, then all genes should have TMRCA that is similar – dating to the split between the two populations (at time t).
- if the isolation with migration model is correct then the ability of different genes to move between species is expected to differ depending on the magnitude of Dobzhansky-Muller incompatibilities.
- therefore, some loci are expected to be capable of moving freely between species while others should be prevented from doing so.
- this approach has recently been applied to a number of *Drosophila* species.
- Machado et al. (2002) obtained sequences from 11 loci and rejected the isolation model for *D. persimilis* and *D. pseudoobscura* but not for latter species and *D. p. bogotana*.
- gene flow appears to have occurred during the divergence of *D. persimilis* and *D. pseudoobscura* but it has been highly variable among loci.
- interestingly, genes in genomic regions that are known to contribute to reproductive isolation showed no evidence of gene flow.
- this observation suggests that natural selection can effectively prevent the introgression of alleles between species if there is some reduction in fitness in hybrids.

Speciation via cytoplasmic incompatibilities

- in insects, an important contributor to speciation is cytoplasmic incompatibility caused by endosymbiotic bacteria of the genus *Wolbachia*.
 - these bacteria are transmitted from mother to progeny by eggs – there is no transmission through sperm.
 - eggs that carry *Wolbachia* develop normally when fertilized by either infected or uninfected males.
 - however, in a cross between a *Wolbachia*-infected male and an uninfected female, the paternal chromosomes are destroyed or lost early in development.
 - it appears that the sperm in *Wolbachia*-infected males are modified in some manner that the *Wolbachia* in the egg cytoplasm are needed to “cure”.
-
- because of the strong selection against males that do not have *Wolbachia*, the infection sweeps through populations very rapidly.
 - different populations may, however, possess different *Wolbachia* strains.
 - these different strains have independent incompatibility reactions – the eggs and sperm must possess the same strain or there is zygotic mortality.
 - these incompatibilities may play an important role in speciation in insects.
 - how widespread similar infections may be in other groups is unknown.

References

- Marchado, C.A., R.M. Kliman, J.A. Markert, and J. Hey. 2002. Inferring the history of speciation from multilocus DNA sequence data: The case of *Drosophila pseudoobscura* and close relatives. *Mol. Biol. Evol.* **19**: 472-488.
- Presgraves, D.C., L. Balagopalan, S.M. Abmayr, and H. Allen Orr. 2003. Adaptive evolution drives divergence of a hybrid inviability gene between two species of *Drosophila*. *Nature* **423**: 715-719.
- Wu, C-I, and C-T Ting. 2004. Genes and speciation. *Nature Reviews Genetics* **5**: 114-122.