Speciation Genes

(How does one species become two?)
Crown group radiation (~ 965 mya)
what defines a species?

Du Rietz 1930: "... the smallest natural populations permanently separated from each other by a distinct discontinuity in the series of biotypes."

Dobzhansky 1937: "... that stage of evolutionary progress at which the once actually or potentially interbreeding array of forms becomes segregated into two or more separate arrays which are physiologically incapable of interbreeding."

Mayr 1942: "... a reproductive community of populations (reproductively isolated from others) that occupies a specific niche in nature."

Cronquist 1988: "... the smallest groups that are consistently and persistently distinct and distinguishable by ordinary means."
what is a hybrid?
Greek hybrides: “son of outrageous conduct”

- interspecific: same genus different species
- intraspecific: different sub-species within a species
- intergeneric: between different genera

Zonkey: zebra/donkey
Bangal: bengal/siberian
carp B: mix of two genera
Oliver:  
- Walked upright  
- Smoked cigars  
- Drank cocktails (mixed himself)  
- “a smell unlike anything human or chimp”  

(Science, 1 November 1996, p. 727) But DNA testing has finally pegged Oliver as strictly a chimp
Horse = 64
Donkey = 62
Mule = 63
meiotic errors
=> hybrid sterile

Lion = 38
Tiger = 38
Liger = 38
Viable and fertile

Why is the liger so big?

Chromosome number critical to viability (trisomy 21)

Dog = 78
Cat = 38
Inviable combination
Why is the liger so big and the tigon so small?

**GENOMIC IMPRINTING** Lions live in prides led by several adult males. The lionesses mate with each of those males. Each male wants his offspring to be the ones to survive, but the female's genes want multiple offspring to survive. The father's genes promote size of the offspring to ensure that his offspring out-compete any other offspring in the womb at the same time. Genes from the female inhibit growth to ensure that as many offspring as possible survive and that they all have an equal chance. By contrast, tigers are largely solitary and a female in heat normally only mates with one male. There is no competition for space in the womb so the male tiger's genes do not need to promote larger offspring. There is therefore no need for the female to compensate, so the offspring's growth goes uninhibited.
Many hybrids are sterile but have the same chromosome number….. Why?

- structurally are males or females more prone to sterility?
- heterogametic sex most prone? (XY vs XX)
- are certain classes of genes affected (TFs)?
- can “speciation genes” be predicted, do they inherently evolve most rapidly (duplicated genes)?
- can epigenetic mechanisms evolve rapidly?
- why/how this gene? Can speciation be pushed in different ways experimentally by modifying mode of speciation?
modes of speciation

Allopatric: geographically isolated populations

http://evolution.berkeley.edu/evosite/evo101/VC1dParapatric.shtml
modes of speciation

Peripatric: same as allopatric but one population is very small

[Diagram of modes of speciation with illustrations of populations and genetic markers, showing the process of speciation through genetic drift and isolation.]
modes of speciation

Parapatric: no extrinsic barrier to gene flow

*Anthoxanthum odoratum*
modes of speciation

Sympatric: behavioral reduction to gene flow
modes of speciation

speciation in plants

ploidy changes: very prevalent in crop plants, tough to sequence genome
What mechanisms lead to incompatibility between two species?

Pre zygotic isolation
1. behavioral isolation: failure to elicit mating behavior
2. temporal isolation: (plants) flowering time different
3. mechanical isolation: breeding incompatibility
4. gametic isolation: sperm never reach egg or fuse

Post zygotic isolation
1. reduced hybrid viability: embryonic lethality
2. reduced hybrid fertility: mule (chromosome number)
3. hybrid breakdown: 1st generation can interbreed, the progeny of 1st generation feeble
4. single (or few) gene changes in any critical process leading to a fertile adult hybrid
Drosophila are an excellent system to study hybrid effects
$D. \text{mel}$ X $D. \text{sim}$, $D. \text{mar}$, or $D. \text{sch}$
= male inviable, female sterile

$D. \text{sim}$ X $D. \text{mar}$, $D. \text{sch}$
= male sterile, female ok

$D. \text{moj}$ X $D. \text{arz}$
= male sterile, female ok
What are the earliest events in speciation?

Haldane’s rule: heterogametic sex 1st to suffer deleterious effects, assumed to be recessive (usually male).

Predictions:
- genetic differences equal throughout chromosomes (only X seen)
- or
- genetic differences unequal, X rapidly evolving inherently, certain types of genes

(J.B.S. Haldane (1922) Sex-ratio and unisexual sterility in hybrid animals. Genetics 12, 101-109.)

Thomas Hunt Morgan 1910

Female inviability
Dobzhansky-Muller Model (1937 - 1940)

“Root cause of hybrid failure is pairs of genes which interact.”

Dobzhansky–Muller criteria: reduced fitness of the hybrid; functional divergence between the two hybridizing species; and dependence of a pair of genes on each other to cause their incompatibility effects.

A = enzyme, B = protein that breaks down the enzyme
A & B => C & D (one population) or A & B => E & F (other population)
C & D or E & F interact fine since they evolved together, but C & F or E & D cannot function properly, thus hybrid failure
70 years later.....

Two Dobzhansky-Muller Genes Interact to Cause Hybrid Lethality in Drosophila

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1

*D. melanogaster* female X *D. simulans* male = no sons

**A**

- Ancestral species
- Independent divergence in each species
- Deleterious interaction in hybrids

KO *D. simulans* Lhr or *D. melanogaster* Hmr = suppresses hybrid male lethality
  (dominant interaction)
What are *Hmr* and *Lhr*?

**Hmr:**
- X chromosome gene
- High sequence similarity to myb/SANT DNA binding domain, and two MADF domains
- Rapidly evolving, lots of nonsynonymous changes

**Lhr:**
- Chromosome II
- BESS domain (interacts with MADF domain)
- Also rapidly evolving
- ~90% AA identity between *D. mel* and *D. sim*, whereas Lhr only ~80%
- Also interacts with HP1, a heterochromatin maintenance gene
Ratio of X chromosomes determines sex, not presence of Y

Male progeny receive X (one total) from mom, and Y from dad

Thus only males receive only *D. mel* Hmr and *D. sim* Lhr

What would the reciprocal cross generate?
Future directions:

What about protein complex formation is deleterious?

What caused the rapid evolution of these genes?
Triploid *D. mel* females X heavily irradiated *D. sim* males

Some lived and were viable

Female “tiny dot” 4th chromosome (of *D. sim*) in an *D. mel* background

Crossing this “tiny dot” line with *D. sim* lead to sterile male hybrids homozygous for the 4th “tiny dot” *simulans* chromosome

Sperm were immotile
2

*JYAlpha*, a Na/K ATPase essential for male fertility was the reason

*JYAlpha* is on the 4\textsuperscript{th} chromosome in *D. mel* but the third in *D. sim* “tiny dot”

Thus hybrids are sterile as they lack *JYAlpha* (possess two “tiny dot” 4\textsuperscript{th})

Replacing with a new *simulans* 4\textsuperscript{th} restores fertility, thus not due to irradiation

Not many ideas for future work in this scenario
The Normal Function of a Speciation Gene, *Odysseus*, and Its Hybrid Sterility Effect

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*D. simulans* X *D. mauritiana* = male sterility, females ok

*Odysseus* (OdsH): rapidly evolving homeobox gene, evolving away from ancestral embryonic function toward predominantly spermatogenic expression, misexpressed in testis

Sterile hybrid  
Fertile non-hybrid
-When *OdsH* KO in *D. mel*

Sterility disappears in 5 day old males, probably normally enhances fertility in young males

*** *OdsH* arose from gene duplication in *Drosophila*, paralog *unc-4* nearly identical in all *D. melanogaster* subgroup species
-argues for duplicated gene => rapid divergence => speciation

Future: try to examine why male sterility often first (early) mechanism of post-mating reproductive isolation
Hybrid lethality when *D. simulans* allele of Nup96 is combined with a hemizygous *D. melanogaster* X-chromosome.

Nup98-Nup96 a dicistronic single copy gene: two members of nuclear pore complex, found on chromosome 3

Thus males with *D. mel* X chromosome and *D. sim* 3rd chromosome die, females ok (one X from each species)
Rapid functional divergence between both species *Nup96* gene

Why does this seem strange?

Studying 5 members of the nuclear pore complex (~30 total): all have very high levels of divergence, in both species

The NPC is largely conserved throughout eukaryotic evolution
Why would the NPC evolve?

1. Genetic conflict between host and pathogen
2. Genetic conflict over centromeric drive
Is there an easier way to find genes that may be incompatibility genes, or on the way to becoming incompatibility genes?

What genes would you predict to be misexpressed?
Many hybrids are sterile but have the same chromosome number….. Why?

- heterogametic sex most prone (XY vs XX) ?

- are certain classes of genes affected (TFs & male specific genes)?

- can epigenetic mechanisms evolve rapidly (near heterochromatin)?
Use microarray technology to examine mRNA levels of genes between pure species and hybrids.

Look in particular at male specific genes.

*D. simulans* X *D. mauritiana* or *D. sechellia* leads to sterile F1 males.
30 genes overexpressed and 190 genes underexpressed using *D. mel* microarray in *sim-sec* hybrids

63 genes overexpressed and 505 underexpressed using *D. mel* microarray in *sim-mau* hybrids

128 underexpressed in both and 4 overexpressed in both
16.7% of genes on array are on the X-chromosome, yet only 9.1% (sim-sec) and 6.2% (sim-mau) were misexpressed X-chromosome genes.

Interestingly, 55% of sim-sec and 34% of sim-mau misexpressed on the X-chromosome were overexpressed, versus ~9% on autosomes that were overexpressed.

Transcription factors were underrepresented: 7% of genes but only 2.2% (sim-sec) and 1.6% (sim-mau).

DNA binding: 6.4% of genes but only 1.4% (sim-sec) and 2.4% (sim-mau).
Chaperones were found 4.3 times more than expected

Protein folding genes were found 4.5 times more than expected

Mitochondrial transport were found 5.2 times more than expected

MAPs were found 3.6 times more than expected

Apoptosis genes were found 3 times more than expected

In testis-specific genes transcription factors were at expected levels and DNA binding genes were overrepresented

Misexpression was more common in adults than in larvae
FIG. 2.— The spermatogenesis pathway (adapted from Fuller 1998; White-Cooper et al. 1998, 2000). Color-coded arrows represent genes significantly misexpressed in hybrid male third instar larvae using the sperm array (purple), 4-day-old adults when assayed using the sperm array (green), or genome-wide array (orange). Lighter shaded arrows on the left are for sim–sec hybrids; darker shaded arrows on the right are for sim–mau hybrids. Underexpressed loci are shown as standard arrows, whereas loci that are overexpressed have an arrow beginning with a circle.
Future work not just examining discovered hybrid incompatibilities

Can speciation events be induced in lab by modifying simple conditions?

Diane Dodd:
Can still interbreed but choose not to unless forced
Conclusions: trends not always followed, why not? What drives the selective pressure of rapidly evolving genes?

- Populations diverge (interbreed very infrequently)
- Opportunities for interbreeding are hindered by sexual selection
- Further divergence with inherent rapid evolution of genes on the X-chromosome (transcription and non-transcription factors)
- Divergence primarily affects heterogametic sex and sex-specific processes
- Early speciation leads (in *Drosophila*) to male sterility
- This further hinders interbreeding and promotes speciation
- Latter events of speciation push divergence further = Male hybrids inviable/female sterility (leads to non-X genes becoming divergent and incompatible)
- Inability to hybridize (all offspring inviable)
- Much later = divergence of chromosome number