I hope you read this story, and more importantly, watched these videos. You might think “this won’t be on the quiz” but some of it will. When I ask you to “Use examples to help explain …”, these readings and videos give great examples and explanations that will help you understand the lecture material and build better answers to the quiz questions.

9/11 Evolution of populations II
Read: Text Ch 20
Read: HUMANS EVOLVING MORE RAPIDLY THAN EVER
Watch: The biology of skin color
Watch: Got Lactase?
Watch: Natural Selection in Humans
Watch: Are We All Related?

Just for fun: Howdy Doody Show, The (Intro) S1 (1947)
Overview of Lecture: Microevolution II

Bullet Points:
• strong inference, null models & Hardy-Weinberg
• causes of deviations from HW: microevolution
• causes of microevolution
• can we freeze evolution in captive (not-frozen) populations?
• MHC, natural selection & mate choice (Smell Dating!)
• Out of Africa – serial bottlenecks and rapid local adaptation
• Dairy farming, culturing cheese and evolving lactose tolerance
• Shared ancestry vs racial categorization by skin color

Evolution in Action
Elizabeth Culotta and Elizabeth Pennisi
Science 23 December 2005: 1878-1879. [Full Text »]

Today evolution is the foundation of all biology,

... At some level every discovery in biology and medicine rests on it.
Learning Goals:

1. Understand and be able to use examples to explain … What is the Hardy-Weinberg equilibrium? How is it used as a null model? Describe five processes that can put a population’s gene frequency out of H-W equilibrium.

2. Be able to use examples to help explain how and why natural selection for survival and sexual selection for mate choice can result in humans being out of Hardy-Weinberg equilibrium at loci for MHC phenotypes.

3. Explain …the “Out of Africa” hypothesis for the phylogenetic-geographic history of modern humans (*Homo sapiens*). Use the example of the independent evolution of persistence of milk digestion (lactose tolerance) into adulthood in herder populations in northern Europe, East Africa and the Middle East, to illustrate the origin of locally-adapted genetic differences among different ancestral lineages of modern humans.
Scientific explanations must adhere to criteria such as:
a proposed explanation must be logically consistent;
it must **abide by the rules of evidence**;
it must be open to questions and possible modification; and
it must be based on historical and current scientific knowledge.

The Rorschach test is a psychological test in which subjects' perceptions of inkblots are recorded and then analyzed …

People imagine patterns and make up stories.

Before we go to a lot of effort to build a scientific explanation for a pattern, we’d like to be confident that there really is a pattern we could explain scientifically. What this means is we want to first …

Of course there is are reasons that cloud looks like a face but we have no real hope of explaining the processes with enough precision and accuracy to predict and explain it scientifically.
“Strong inference” requires that we reject alternative hypotheses.

If we can reject the null hypothesis that the observed pattern is just the result of random, unexplainable processes, then we can infer that some non-random causal process is at play, and further investigation is warranted, to determine what that process is.

There are many different kinds of ‘random’ processes

If we observe from a sample of data that one outcome (yes, win, head, allele-A, etc) occurs $x$ times out of $n$ possible times (‘Bernoulli trials’) then we say that that outcome has observed probability or relative frequency: $p_{\text{obs}} = x / n$.

Imagine flipping a coin $n$ times and observing $x$ heads out of $n$ flips. Our null hypothesis is that it is a “fair coin” with $p_{\text{exp}}(\text{head}) = 0.5$. If the null hypothesis is correct, than over many experiments we expect to observe $x/n \sim 0.5$, probably, most of the time, but not always exactly 0.5.
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By ‘test the null hypothesis’ we mean use statistics to figure out the probability that we would get the observed pattern = the data = observed $p_{obs}$ if the underlying process were ‘random’ with actual expected $p_{exp} = 0.5$.

Suppose we do an experiment to test the hypothesis that a coin is “fair” with $p_{exp} = 0.5$. Suppose we’re lazy or in a hurry and the experiment involves flipping the coin 4 times. Suppose that we observe 4 heads in a row: $x/n = 4/4 \rightarrow p_{obs}(\text{head}) = 1.0$. Would you infer that this is NOT a fair coin?

What is the probability of flipping 4 heads in a row?

$\frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} = \frac{1}{16} = 0.0625$

What if 5 heads in a row?

In journal articles, this is written as ‘$p < 0.05,$’ where 0.05 = 1/20. - very conservative!

Suppose: flip 4 heads in a row; $p_{obs} = 1$. Reject the null hyp “it’s a fair coin”?
Suppose we have two coins \( \bigcirc \bigcirc \); & we want to test whether they are both “\textit{fair}” (long-term ave \( p(h) = 0.5 \)) & \textit{independent} of each other.

Experiment: flip both, record combination, repeat \( n \) times \( (n \text{ is big}) \) …

If the NULL MODEL (two “\textit{fair}”=\{\( p(h)=0.5 \) \} \& \textit{independent} coins) is correct then the pattern/data we would expect to find across 1 experiment (in a big sample) is:

\[
\begin{align*}
p(hh) &= p(h)p(h) = 0.5 \\
p(ht \text{ or } th) &= p(h)p(t) + p(t)p(h) = 2pq \\
p(tt) &= p(t)p(t) = q^2
\end{align*}
\]

\[
\begin{align*}
\text{If we ignore the source of the } h \text{ & } t & \text{ (the color of the coin), then } p(1h & 1t) = p(h)p(t) = pq\
\end{align*}
\]

More generally, if \( p(h) = p \) and \( p(t) = q = 1-p \), then expect (null model)

\[
p(hh) + p(ht \text{ or } th) + p(tt) = 1
\]

\[
p^2 + 2pq + q^2 = 1
\]

Suppose we find (data): \( p(h) = 0.5 \), but rel. frequency hh = \( p(hh) = 0.1 \)?

This is why you need statistics!
Say kids, what time is it?

**It’s Hardy-Weinberg Time!**

[https://www.youtube.com/watch?v=pnUGAe0yqz4](https://www.youtube.com/watch?v=pnUGAe0yqz4)

Buffolo Bob, speaking:
Ah, yes sir, and boys and girls all over America
and kids here in Doodyville
and Grand Rapids, Michigan,
let's go!

Everyone sings:
It's Hardy Weinberg Time.
It's Hardy Weinberg Time.
Hardy and Weinberg Do
Say Howdy Do to you.
Let's give a rousing cheer,
Cause Hardy-Weinberg’s here,
It's time to start the show,
So kids let's go!

March 6, 2015

The original Howdy Doody marionette from the 1940s
will be among the puppets of distinction
going on display at the Detroit Institute of Arts.
Suppose we have two copies (diploid) of a locus \( \square \square \); w/ 2 alleles: \( B \) \( b \) & over the pop of \( n \) individuals (2n loci): \( p(B) = p = 0.6 \) & \( p(b) = q = 0.4 = 1 - p(B) \)

& we want to test whether the alleles assort randomly and independently

Experiment:’ meiosis, sex & recombination \( n \) times (\( n \) is a big population) …

If the NULL MODEL (“random & independent sorting”) is correct then the pattern/data we would expect to find across 1 generation (in a big sample) is:

\[
\begin{align*}
p(\text{BB}) &= p^2 = 0.6 \times 0.6 = 0.36 \\
p(\text{Bb}) &= 2pq = 2 \times 0.6 \times 0.4 = 0.48 \\
p(\text{bb}) &= q^2 = 0.4 \times 0.4 = 0.16 \\
p(1)(\text{B}) &= \frac{1}{1} = 1.00
\end{align*}
\]

This particular NULL MODEL (for ‘random’ survival & sex) is called:

The Hardy-Weinberg equilibrium

If we ignore the source of the \( B \) & \( b \) (parent: mom or dad), then \( p(1)(\text{B}) & 1(\text{b}) = ? \)

Suppose we find (data): \( p(b) = 0.4 \), but \( p(\text{BB}) = 0.55 \) ?

What might cause deviation from H-W eq?
What processes would cause a pop to evolve at a locus (& lead us to reject the H-W null model)?

1. Mutation – like 'gene flow from another dimension'
   - In theory, always invalidates H-W, but relatively weak and non-directional.
   - but consider: selection for more or less mutation repair?

2. Gene flow – immigrants (or gametes) with different allele frequencies make the p & q of the breeding adult population different from the p & q of the ‘native born’ population
   - Consequences can look similar to selection.
   - bottleneck-founder effects important in island speciation
   - accumulation of neutral mutations over time since common ancestry, including in human species as we spread across earth

3. Non-random mating – including because of sexual/social selection
   - assortative:  \( p(BB) > p(B) \times p(B) \), ‘too many’ homozygotes
   - disassortative:  \( p(Bb) > 2 \times p(B) \times p(b) \) ‘too many’ heterozygotes

4. Selection – systematic differences in genotypes of breeders relative to initial whole population of potential breeders resulting in change in p & q of next generation.
What does it mean to “freeze evolution” and why would it be difficult in this panda example?

A single generation of domestication

Evolutionary genetics of the major histocompatibility complex. 
HEDRICK PW. 1994. AM. NAT. 143: 945-964.

The major histocompatibility complex (MHC) – aka HLA (genes code for molecules that present antigens to the immune system) 
... was first studied because of its importance in tissue transplantation and the immune system in humans. ... over 80 genes in the MHC, ... and, in some populations, there is an observed deficiency of homozygotes. 

... some type of selection is operating in this region. 

... this selection is related to the basic role of the MHC as part of the immune system acting to suppress attack by viruses, bacteria, and other parasites. 

... research suggests that there is selection at the MHC involved with maternal-fetal interactions {selective spontaneous abortion -miscarriage} and nonrandom mating.

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Americans who are heterozygous for HLA-A, -B or -C antigens are protected against rapid progression to AIDS {HLA is MHC in humans} after infection with the human immunodeficiency virus-1 (HIV-1).

for a good overview, see:
The evolutionary ecology of the major histocompatibility complex 
Human leukocyte antigen matching and fetal loss: results of a 10 year prospective study. 

... it has been suggested that (histocompatible) fetuses whose HLA alleles do not differ from maternal alleles are more likely to be aborted [spontaneous miscarriage] than (histo-incompatible) fetuses with HLA alleles that differ from maternal alleles.

We conducted a 10 year prospective study of HLA matching and pregnancy outcome in 111 Hutterite couples, providing information on 251 pregnancies. A logistic regression analysis was performed to determine the effects of HLA matching at HLA regions and loci on pregnancy outcome (fetal loss versus delivery). Significantly increased fetal loss rates [miscarriages] were observed among couples matching for the entire 16-locus haplotype ($P = 0.002$). Among the individual loci, loss rates were increased among couples matching for HLA-B ($P = 0.019$), HLA-C ($P = 0.033$) and the complement component, C4 ($P = 0.043$).

We interpret these results as evidence that matching for the entire 16-locus haplotype confers significant risk for fetal loss [selective spontaneous miscarriages].
MHC-dependent mate preferences in humans. 

One … benefit of sexual reproduction could be that it allows animals (including humans) to evolve rapidly to a continuously changing environmental selection pressure such as coevolving parasites.

This … would be most efficient if the females were able to provide their progeny with certain allele combinations for loci which may be crucial in the parasite-host arms race, for example the MHC (major histocompatibility complex).

Female and male students were typed for their HLA-A, -B and -DR.

Each male student wore a T-shirt for two consecutive nights.

… each female student was asked to rate the odours of six T-shirts.

MHC-correlated mate choice in humans: A review 
Havlicek & Roberts. 2009 - most odor-based studies demonstrate disassortative preferences
Smell dating: sniffing out potential lovers (and their sweaty T-shirts)

The first ‘mail odor dating service’ matches people based on a three-day old T-shirt sample. If both your nostrils agree the other smells great, it’s a match.

https://smell.dating

HOW DOES IT WORK?

A new dating app claims the key to finding your soul-mate is by the way they smell

You pay $25 and receive a t-shirt in the mail: Wear the shirt for three days in a row, but refrain from showering or applying deodorant. However, smoking and sitting by a campfire are acceptable.

After wearing the shirt for 72 hours, send it back to Smell Dating: After you’ve returned your shirt, Smell Dating will send you 10 shirts from other people who have also spent the last 72 hours wearing them without showering.

If you like the smell of any of the shirts (and they like yours too), Smell Dating will give you each other's phone number: Unlike Tinder, eHarmony and all of the other dating sites, Smell Dating does not ask about your sexual preference, what gender you are, if you like long walks on the beach or if you’re a vegetarian.
Most people understand how natural selection drives evolution. Less well known is that sexual selection can sometimes have an even bigger influence on how species evolve. Darwin figured this out first and said it best.

"He who admits the principle of sexual selection will be led to the remarkable conclusion that the nervous system not only regulates most of the existing functions of the body, but has indirectly influenced the progressive development of various bodily structures and of certain mental qualities."

"Courage, pugnacity, perseverance, strength and size of body, weapons of all kinds, musical organs, both vocal and instrumental, bright colors and ornamental appendages, have all been indirectly gained by the one sex or the other, through the exertion of [social and mate] choice, the influence of love and jealousy, and the appreciation of the beautiful in sound, color or form and these powers of mind manifestly depend on the development of the brain."

[We’ll look at “Evolutionary Psychology” later in the course]
Genetic and paleoanthropological evidence is in accord that today’s human population is the result of a great... expansion [Out of Africa] that began approximately 45,000 to 60,000 y ago in Africa and rapidly resulted in human occupation of... the Earth’s habitable regions. ... this expansion was accompanied by a continuous loss of genetic diversity, a result of what is called the “serial founder effect.”

This particular population history gave rise to the two defining features of genetic variation in humans: ...

These two patterns are relevant for medical genetic studies mapping genotypes to phenotypes and for inferring the power of natural selection in human history. ...
Archaeology: **The milk revolution**

When a single genetic mutation first let ancient European adults digest milk, it set the stage for a continental upheaval.

During the most recent ice age, milk was essentially a toxin to adults because unlike children they could not produce the **lactase enzyme** required to break down lactose, the main sugar in milk.

This **two-step milk revolution** {1st “nurture” then “nature”} may have been a prime factor in allowing bands of farmers and herders from the south to sweep through Europe and displace the hunter-gatherer cultures that had lived there for millennia. {note: immigrants displaced locals} continued …

See: www.hhmi.org/biointeractive/making-fittest-got-lactase-co-evolution-genes-and-culture
The milk revolution continued …
Most people who retain the ability to digest milk as adults can trace their ancestry to Europe… where the trait seems to be linked to a single nucleotide in which the DNA base cytosine changed to thymine …
There are other pockets of lactase persistence in West Africa, the Middle East and south Asia that seem to be linked to separate mutations. \{ indep. convergence \}

The single-nucleotide switch in Europe happened relatively recently.
Researchers estimated the time by looking at genetic variation in modern populations and running computer simulations of how the mutation might have spread. … the lactase persistence LP allele, emerged about 7,500 years ago in Hungary. Once the LP allele appeared, it offered a major selective advantage. In a 2004 study, researchers … called that degree of selection “among the strongest yet seen for any gene in the genome”.

As agriculture spread from Anatolia to northern Europe over roughly two millennia, … domesticated cattle at Neolithic sites in Europe were most closely related to cows from the Middle East, rather than indigenous wild aurochs. … incoming herders brought their cattle with them, rather than domesticating locally … \{ immigrants replaced locals \}
A similar story is emerging from studies of ancient human DNA … which suggest that Neolithic farmers in Europe were not descended from the hunter-gatherers who lived there before. \{ immigrants replaced locals that’s how allele spread \}
In the wake of the sequencing of the human genome in the early 2000s, genome pioneers and social scientists alike called for an end to the use of race as a variable in genetic research. [Race] has historically been used as a taxonomic categorization based on common hereditary traits (such as skin color) to elucidate the relationship between our ancestry and our genes. 

[but skin color is a convergent trait, under selection by sunlight-UV, that is poorly correlated with ancestry and overall genotypic similarities ]

We believe the use ...race in human genetic research ... is problematic ... It is time for biologists to find a better way. It is important to distinguish ancestry from a taxonomic notion such as race. 

Ancestry is an individual's relationship to other individuals in their genealogical history. Race is a pattern-based [taxonomic] concept ...which connects an individual to a larger ... socially constructed group.

... phylogenetic and population genetic methods do not support a priori classifications of race ...

We propose ... Scientific journals should encourage use of terms like “ancestry” or “population” to describe human groupings in genetic studies and should require authors to clearly define how they are using such variables.