Some Genetics Background 1

- Within anthropology, it is the field of molecular anthropology that focuses on these issues:
  - What is our genetic relationship to non-human primates?
  - How can genetics help us trace the history of human migration?
- mtDNA
  - I want to reenter the genetics discussion is at the point of the mitochondrial DNA (mtDNA). The mtDNA generates the energy inside the cell.
  - mtDNA is the circular DNA located in the mitochondria of the cell.
  - We receive our mtDNA from our mothers.
  - This means that all the mtDNA in the world originated with a single woman (the mitochondrial Eve).
  - Subsequently, the copies in ancestors mutated so that today there are many variants.
  - Remember all started with one woman, mutated into many forms.
  - Even so, remember your specific mtDNA is from only one of those variants and only from one of your ancestors (our mother’s mother’s …… mother).
  - A term to know is coalescence (the tracing of many peoples’ DNA back to a sequence in a single person).
- Y-chromosome
  - The Y-chromosome is a similar process for men as we talked about for women (with the obvious difference that men have mtDNA from their mothers, but women do not have a Y-chromosome).
  - The other DNA, because of the nature of inheritance, is more difficult to use for tracing common human ancestry.

Some Genetics Background 2

- Mitochondria: Why do researchers target mtDNA?
  - The mtDNA is 16,569 nucleotides (37 genes) long; thus its much smaller size makes it attractive to those doing genetic work linked to migrations.
  - Further, there is less risk that this mtDNA will get tangled, a common problem in nuclear DNA and which is called crossing over.
  - The last attraction of mtDNA is that is no/little effect from natural selection.
- From where did the mitochondrion come?
  - Many researchers have suggested that the mitochondrion was once a free-living bacterium.
  - Then along the evolutionary way, a multi-cellular organism failed to completely phage (read eat) the ancestral bacterium.
  - The two organisms formed a symbiotic (or even parasitic) relationship. This idea is called the endosymbiotic theory.
  - How mitochondria resemble bacteria?
    - Their shape and size.
    - How they divide.
    - They have two membranes. Suggested the outer one from the engulfing organism, the other original to the mitochondrion.
    - Some enzymes and inner membrane transport systems similar.
    - Both mitochondria and bacteria have a circular loop of DNA.
    - They produce some proteins using their own ribosomes.
    - Their ribosomal RNA is similar.
    - Mitochondrial division resembles bacterial binary fission.

Some Genetics Background 3

- Timing
  - We can trace the mitochondrial Eve to about 200,000 years ago and the Y-chromosomal Adam has recently been recently (March 2013) dated to about 338,000 years ago.
  - The Y-chromosome may (or may not) have also coalesced at the same time as the mtDNA.
• Why this happened is predicted to be due to what is called a bottleneck.
  • Bottlenecks occur when the population is very small.
  • This means isolation results in greater similarity within the group.
• One famous case of inbreeding was found among the Hapsburgs, which resulted in the presence of the Hapsburg lip. Read more on this, including a pedigree chart at this link.
  • The Hapsburgs of Austria-Hungary were similar to a small ‘village’ of marriage partners.
  • Many famous family members: Marie Antoinette, for one.
  • The Hapsburg family was endogamous (they married within family or caste).
    • Using endogamy as a tool, geneticists can get some information concerning how people are related to each other.
    • Even if the person is of unknown ancestry, we can estimate: 1) likely region of origin and 2) maybe even where the ancestors lived.
    • The opposite practice of endogamy is also practiced: exogamy (marrying out).
  • In the U.S. we tend to practice homogamy (same education, religion, ethnicity).

Some Genetics Background 4
• There is a common mathematical exercise where we determine the number of grandparents we have. Math: basically $2^x$, where x is number of parental generations
  • Think: 46 chromosomes and 1024 ancestors at 10 generations.
  • Being descended from someone does not mean you have any of that person’s DNA!
  • So, while the mtDNA is traced to a single ancestral line, the vast majority of our nuclear DNA is accumulated from a wide selection of people in our past.
• Remember that we are more closely related to each other than we tend to think.
  • Lots of second cousin marriages are one reason why.
  • At 10 generations back we all have ‘circles of inheritance’.
• Generally Americans are unaware of the circles, but genealogical research turns up these circles.
  • Think of the example of our presidents.
  • I can give my mom’s knowledge as another. She knows all my relatives who married whom and such (my family is from a small, rural town).
  • One interesting statistical model that tries to estimate the degree of relatedness was created by Joseph Chang, this model assumes random matting, but suggests:
    • An ancestor from a region has a 80% chance of having descendants in a region (or 20% the ancestor’s lineage went extinct).
    • That from a genetic perspective, one marries the entire family, So, if a foreign traveler moves into a region 800 years ago, his/her genes (via their children) could be co-mingled with all others in the region.
    • According to Chang, the further you go back in time, the greater the sharing of genes across regions. At 1600 years ago, one’s genes are co-mingled across the Old World.

The Apportionment of Variation 1
• Introduction
  • Goodman, et al. in this chapter are concerned with a discussion of the structure of human genetic variation and phenotypic variation (how we look as a result of genes and environment).
  • We have discussed that variation tends to be continuous and that the geographic variation in one trait is structured or patterned differently than that of another trait.
  • We saw this when we discussed skin color and sickle cell anemia.
  • We are going to discuss one issue even deeper: Whether genetic variation is apportioned along “racial lines”. Does race explain the structure of human variation?
  • We will also glance at the history of the study of apportionment of human variation and of evolution that shaped current distribution.
  • We will also delve into a recent find on the preponderance of variation in Africa.
• Ashley Montagu and the Man’s most dangerous myth: The fallacy of race
  • Montagu was born in England but trained as an anthropologist in the United States.
• His famous work, *Man's most dangerous myth: The fallacy of race*, was first published in 1942, at the height of the Nazi atrocities. [FYI: Goodman et al. mislabel the work as *The myth of race*.]

  • He was influenced by two of the premier anthropologists of all time: Bronislaw Malinowski and Franz Boas, as well as the sociologist, W.E.B. Du Bois.
  
  • In particular, the tutelage of Boas is reflected in this work.
  
  • His premise seems obvious to us now, but at the time the concept that race was a cultural construct was not widely discussed.

The Apportionment of Variation 2

• Ashley Montagu and the *Man's most dangerous myth: The fallacy of race*

  • He went to explain that as a system of classification it failed to differentiate between biological and cultural terms.
  
  • Even after he wrote this book, other anthropologists continued to insist that race was biologically real (remember Coon and Garn?).
  
  • In addition to arguing against racial types, he showed that physical traits are discordant.
  
  • Montagu did not get everything right.
  
  • Due to his lack of genetic-based data, he blurred the lines between race as a cultural construct and that of race as a biological construct.
  
  • Therefore, he advocated the dismissal of race as biological (a modern view), but also that it is not a reality as a cultural construct (an error).

• Richard Lewontin and the apportionment of variation

  • It would take the work of Lewontin to provide the genetic basis for the dismissal of biological races.
  
  • Prior the publication of his work, anthropologists were running around everywhere collecting data on variation in Mendelian traits.
  
  • In particular, blood group variations were an anthropologist’s favorite data.
  
  • Of course anthropologists were not the only ones. Remember Cavalli-Sforza?
  
  • Lewontin was particularly interested in determining the OVERALL pattern of human variation rather than that for a particular trait.
  
  • He wanted to determine how much variation was determined by race, both within a population and between populations.
  
  • In his now famous publication in 1972, *The apportionment of human variation*, he reported that the average variation among 17 blood groups was almost all local.

The Apportionment of Variation 3

• Richard Lewontin and the apportionment of variation (continued)

  • His findings remain one of the most influential today, with many researchers repeating his work.
  
  • Depending on the set of traits used, the values vary a bit, but the overall interpretation continues to be supported.
  
  • He compared three categories: “variation within a population”; “variation between populations, but within a race”; and “variation between races”.
  
  • The greatest degree of variation was within a single population.
  
  • He reported that some variation between populations, but within a “race”.
  
  • Only about 6-10% between what are called “races”.
  
  • To the right is a set of diagrams that illustrate this change in paradigm.
  
  • The essentialist model is another term for typological model. It acknowledges some overlaps, but at its “core” there are true racial differences.
  
  • The population model suggests even greater overlap between the groups once called races, does not suggest an essential difference in population, but suggests historically some traits are seen as distinctly different.
  
  • Lewontin’s model represents the genetic reality. Mostly “races” overlap; the center of variation in one group is nearly the same as the other groups. Race is not a genetic reality, even as we insist on it culturally.

The Apportionment of Variation 4

• An interview with Richard Lewontin

  • Does racial difference exist on a genetic level?
• Because humanity has occupied many different geological regions they do look different from each other. There is this kind of genetic differentiation (he means superficial differences).
• The real question is not whether these differences in hair color or skin color are genetic, they are. The real question how much the differences in OTHER genes is dependent on these easily observable genes?
• He asks whether there are a lot of genes that separate those groups.
  • Stephen Jay Gould would ask, “Is there something called a ‘race gene’?”
  • We know the answer is no.
• He reminds us that there is polymorphism (variation) in the ABO blood group. [Of course there is variation in most of our genetic traits.]
  • Blood was of particular importance to anthropologists as they could assess genetic data from a single blood draw (today, a cheek swab).
  • Lewontin stated, “Anthropologists just went around the world taking blood out of everyone” (p.125). It’s true!
• You can not really tell the difference between populations using the ABO group, but there are some blood groups where this is not true. He suggests the Duffy blood group (but that is linked to malaria adaptation).
• Lewontin now estimates that only 7% of the differences in humanity are between Africans, Asians, North Americans, Austro-Asians, and so forth. Additionally, he estimates that 75% of our genetic make-up is essentially (or nearly essentially) identical.

The Apportionment of Variation 5
• An interview with Richard Lewontin
  • How do you measure human genetic variation?
    • One measures the variation by looking at all the different variants of a gene (alleles) and then we calculate the percentages for each allele (allelic frequency).
      • Scenario 1: If the relative frequencies between two populations is the same, say 99% of allele 1 and 1% of allele 2, there is no variation BETWEEN populations.
      • Scenario 2: If the relative frequencies between two populations is the same, say 1% of allele 1 and 99% of allele 2, there is significant variation BETWEEN populations.
    • In Scenario 1 there is no difference BETWEEN populations but there is difference WITHIN the population. And Scenario 1 is much more often the case than Scenario 2.
  • So what did you discover about population differences?
    • In Scenario 1 there is no difference BETWEEN populations but there is difference WITHIN the population. And Scenario 1 is much more often the case than Scenario 2.
      • So what did you discover about population differences? At the start of his work, Lewontin had to address the issue that studying genetic diversity meant trying to connect genetic diversity to outward manifestations (how we look). Also, most genes do not have an outward manifestation.
      • For a long time, we did not realize how much variation existed between individuals.
      • Lewontin began using gel electrophoresis to measure variations in proteins (migrate based on size, shape and chemical charge).
        • He learned that about 25-33% of genes vary.
      • Subsequently he shifted from the level of proteins to the study of DNA

The Apportionment of Variation 6
• An interview with Richard Lewontin
  • So how much difference is there between human groups?
    • Generally speaking:
      • First, ~75% of all our genes are the same for all of humanity, with extremely rare exceptions.
      • For the remaining 25-33%, the proportions between populations are the same, if 50/50 in one population, you see 50/50 in the others.
      • For a few genes, such as Duffy, there is great diversity, but this is a rare observation.
    • So here is the breakdown:
      • The first ~75% of all human genes are essentially the same.
      • Among those genes that remaining:
• The variation WITHIN a population represents 85% of the total.
• Of the remaining 15%, about 8% is BETWEEN populations within a region, and about 7% represents differences across “races”.

• What does this tell us about race?
  • We found no major differences between groups. Race is not a valid biological term.
  • He concurs with race as a social construct.
• Why do people still hold on to biological explanations of difference?
  • Because race is a social reality.
  • We use race to avoid addressing social injustices; to validate the inequality.
• What is the relationship between your DNA and how to turn out as a person?
  • Instructor comment: This is the classic nature/nurture question.
  • He reminds us this is a phenotype/genotype query. There is no simple one-to-one for most traits (he is talking about Mendelian traits).

The Apportionment of Variation 7

• An interview with Richard Lewontin

  • What is the relationship between your DNA and how to turn out as a person? (continued)
  • He stories about the Dionne Quintuplets who are genetic clones of each other, and who grew up in the same house, dressed the same and so forth.
  • Once they left home, their lives took very different trajectories.

• Aren’t groups of Icelanders genetically distinct because they’ve been more isolated?
  
The Icelandic government recently sold the country’s entire genome to a private company (deCODE Genetics).
  • This original company went bankrupt and was bought by Amgen in 2012; Amgen is an American biotechnology company (one of the largest).
  • When under the control of deCODE Genetics, there was interest in Iceland because of the perceived uniqueness of their genetics.
  • They were thought to be relatively homogenous due to the vagaries of history (limited migration from Norway and a subsequent famine), but are they a genetic isolate?
  • Nope they were traveling around (pirating and co-mingling).
  • Research on their genetics shows they are not much more homogeneous than other Europeans with which they were compared
  • Myriad Genetics, an American company, claims the patent on the BRCA-1 and BRCA-2 genes because they isolated them.
  • These genes are linked to an increased risk for breast and ovarian cancers.
  • This case went to the U.S. Supreme Court and in June 2013 the BRCA patent was voided. cDNA can be patented.

The Apportionment of Variation 8

• Updating Lewontin: The structure of genetic variation today

  • Yu et al. reexamined the work of Lewontin and a new model appeared, based on their ability to sequence large sections of the human genome.
  • When they compared groups they labeled as “Europeans”, “Asians” and “Africans” an interesting pattern emerged:
    • They found a pattern of diversity between the first two groups that aligned with Lewontin.
    • When they looked at Africans, the picture shifted.
    • There is more variation between any two Africans than between an African and a non-African. This actually makes sense.

  • Notice that the relative sizes of the circles are not the same?
  • This represents that the diversity within Africa is much greater and also encompasses that found in non-African populations.
  • Also, it reminds us that non-Africans are really subsets of Africans.
  • Before we go on to the next discussion, it is important to remember that human variation is not as extensive as seen in many species.
• The key to all this is that the differences are relatively recent in our human history; the important human traits are old.

The Apportionment of Variation 9
• Lewontin’s Fallacy
  • There is a recent paper published that deeply challenges Lewontin’s interpretation. Edwards argues that Lewontin got his math wrong (simplified statement, but the essence); he calls it “Lewontin’s Fallacy”.
  • Edwards is not the first to challenge Lewontin, many suggest that we can tell differences genetically.
    • One such paper by Health et al. was published in 2008 and claims to be able to see a gradient of traits (read cline) that cluster (read populations).
    • Another by Witherspoon et al. is more complex, but confirms the limited variation between populations AND suggests that with enough data one can be accurately assigned to a population (if you ignore admixture and so forth).
    • Svante Paabo argues that the clusters are the results of ignoring the need for proper sampling and that when you do you see gradients (read clines) and not clusters.
  • All are discussing genetic distances AND whether they are discrete (races) or gradient (clines).
• Lessons learned?
  • 1) Avoid sampling errors.
  • 2) Do not ignore admixture (it represents the reality of humanity).
• Perspectives on genetic genealogy (moved here from Chapter 11)
  • Some of the kits available commercially test mtDNA and others the Y-chromosome.
  • Among the best known are those available from 23andMe and the Genographic Project.
    • Click here to read two actual examples persons who solicited their DNA data from the Genographic Project: male and female.
    • Their names are removed of course, for the sake of privacy.

The Apportionment of Variation 10
• Perspectives on genetic genealogy (continued)
  • The degree of relatedness of populations can be shown visually, and is called is called a genetic tree.
  • It is important to remember that these trees are often describing the variation of a few genes and that it can get very messy very fast when more genes are added.
  • Remember, we can be fairly sure of who was our mother, but biologically less sure of paternity
    • Nonpaternity
      • Medical students are taught that 5-10% of the fathers identified on birth certificates are not the true biological fathers.
      • Geneticists confirm this statement, but the results of the genetic studies are not often published.
      • First-borns and last-borns are more likely to be found to be associated with ‘nonpaternity’
    • Adoptions is another reason that new genes are brought into families
    • Multiple marriages also scramble genealogies.

The Apportionment of Variation 11
• So what do your results really mean? 5 opinions:
  • There are limits: The test only follows a single line of your ancestry (your mother’s mother…. Or your father’s father…). Remember (earlier in lecture):
    • If you go back 800 years, you have 1,024 ancestors.
    • Although not all contributed to your DNA make-up.
  • Recovering the past: For groups of people with little information about their pasts (such as African American descendant of slaves) it can be valuable.
  • A matter of interpretation: It is not uncommon that the consumer of these tests interprets the results to fit their expectations.
  • Claiming identity: Some use to determine their “Native American identity” (in a manner reminiscent of blood quantum, but ignore that being an American American is about culture.
• **Less than advertised:** When the data provided is labeled as “European” or “Native American” and so forth, it fails to address the shared genetic history.

• **So what does all this tell us about our genetic histories?**
  • **First,** most of the groups we belong have nothing to do with biology (at least in the US). Most groups are due to culture, not biology.
  • **Second,** racial and ethnic groups are also cultural products.
  • **Third,** even as we create cultural groups, it is true that there are physical differences between us (just not biologically racial differences, of course).
    • Our species is too young to have created deep genetic differences.
    • Geneticists have never found a mutation that is 100% present in one ‘race’ or 100% absent in another (there is no such thing as a race gene).