Introduction to Biological Anthropology: Notes 5

Darwin's big problem and Mendelian genetics

- Darwin's big problem
  - We have seen that natural selection works by favoring the most successful variants among the individuals in a population
    - it only works if individuals vary in ways that affect their survival and reproduction
    - offspring must be similar to their parents, but not exactly the same
      - if offspring were identical to their parents, they would be identical to each other, and there would be no "more successful" and "less successful" individuals for natural selection to pick from
      - so there could be no change in the next generation: no evolution
  - Darwin had no good explanation for why offspring vary
    - he knew that this was a big gap in his theory
  - The prevalent idea of inheritance in Darwin's time was "blending inheritance"
    - "blending inheritance" holds that the characteristics of offspring are mixtures of the characteristics of their parents
      - the idea was that the material from the two parents that controlled inherited characteristics blended like two colors of paint
      - this is a reasonable approximation, based on everyday experience
    - so, every mating should produce offspring that are intermediate between the parents
      - for example, if a six-foot man mates with a five-foot woman…
      - then the offspring should all be between five and six feet tall
      - no offspring are expected to be more extreme than either parent
    - there are two huge problems with the blending model of inheritance
      - First, it obviously isn't true
        - lots of parents have children who are taller, or shorter, than both of the parents
        - many kids have traits like hair color, eye color, etc. that neither of their parents have
        - so blending simply can't be what is going on
      - Second, in a few generations, blending inheritance would cause the whole population to be mixed to the same average of all traits
        - the same medium height
        - the same medium hair color, eye color, skin tone, etc.
        - after a while, all the individuals would be the same
        - selection would have no variation to work on
        - and evolutionary change would stop
        - this obviously does not happen, so inheritance must work in some other way
  - So Darwin needed to explain:
    - why do offspring vary?
    - why doesn't that variation get averaged away after a few generations?
    - natural selection weeds out poorer variants, but where do *new* variants come from?
      - That is, if natural selection weeds out some types, why aren't they all eliminated, leaving just the one, best type?

- remember the corn example
  - researchers started with corn kernels that varied from 4% to 6% oil content
  - they picked the oiliest seeds every generation
  - so wouldn't they eliminate all the low-oil variants and end up with a population of only plants that produce 6% oil?
  - No: the oil content kept going up, to over 18%, far oilier than any seed in the starting population
  - where did these new variants come from?
    - more generally, how can a population evolve beyond its original range of variation?
- In short: Why is there variation for natural selection to select from?
- Darwin was fully aware of this problem, and it bothered him

- Darwin published the *Origin of Species* in 1859, and went on working and publishing through 1872 (he died in 1882)
  - He was unaware that the one serious problem with his theory had been solved just a few years after the *Origin* was published
  - By Gregor Mendel
    - a brilliant man, but in many ways the opposite of Darwin
    - born into a poor family
    - like Darwin, went to university (in Vienna), but did not take well to it and quit
    - needed to do something for a living, so he joined an Augustinian monastery in Brno (now in the Czech Republic)
    - Mendel worked as a teacher in the technical institute there
    - taking advantage of the experimental garden at the technical institute, from 1856 to 1863 (starting before the *Origin* was published, and continuing several years after), he systematically studied patterns of inheritance in garden peas
    - Based on his experimental work, Mendel deduced the basic principles of genetics
      - which would replace "blending inheritance"
      - and explain how variation could be maintained in spite of selection
      - and, with some help from later researchers, even explain how "new" variants beyond the range of previous generations could be produced
    - Mendel knew his work was important, and he published it promptly in 1866
      - He had read Darwin's *Origin of Species* and understood that his work filled in the one major gap in evolutionary theory
    - Unfortunately, Mendel used a mathematical approach to his data
      - as you will see, it was simple, and you will understand it
      - but biologists at the time were not ready for this kind of mathematical reasoning
    - and, as you will see, he had to propose "particles" of inheritance (now called genes and chromosomes) that had never been physically observed
      - because they too small to see with common instruments of the time
      - so if you didn't understand his math, it seemed like he was making up pure fantasies
    - Mendel sent a copy of his paper to the biologist Karl Nägeli
      - who ignored it, possibly because it did not support his own ideas, or possibly because Mendel was not a recognized academic

    - Mendel apparently also sent a copy to Darwin
      - a copy of the journal with Mendel’s article was among Darwin’s papers at his death
      - but the folded edges of the pages had to be cut to read the journal
      - some other articles were cut open… but Mendel’s wasn’t
      - the answer was there on his desk, but Darwin never read it.
    - so Mendel’s findings were ignored
      - Darwin died without knowing that the problem had been solved
      - and Mendel gave up biology and went into administration at his abbey
    - Mendel’s work was noticed again around 1900, over 30 years later
      - this time it was accepted, because chromosomes had been seen with microscopes
        - now there was a known physical mechanism by which his model could work

- Mendel’s experiments
  - Mendel wanted to understand how heredity worked
  - so he picked a convenient, easy-to-handle plant: the garden pea
    - with many easy-to-observe, “either-or” characteristics that varied from plant to plant
      - color of flowers: purple or white
      - location of flowers: axial or terminal
      - color of seed: yellow or green
      - shape of seed: smooth or wrinkled
      - color of pods: green or yellow
      - shape of pods: “inflated” or “constricted”
      - height of plant: tall or short
      - [in each of these pairs, the first is dominant and the second recessive]
  - Mendel carefully bred combinations (crosses) of different kinds of pea plants
    - One of his key innovations was to do not just a few, but a large number of these crosses
    - and to count the resulting plants
      - he went through 28,000 pea plants during the course of his study
    - like flipping a coin, the only way to find out how likely each outcome is, is to try it many times and count up the results
    - a small sample won’t give a very good estimate; but a large sample will
  - He noted the proportions of different traits, and realized what they meant
  - Mendel realized that the proportions of plants with different characteristics could be explained by a simple model involving a few rules plus random chance

- Mendel’s model of inheritance
  - inheritance is *particulate* (or “digital”)
    - it is not based on a substance that blends like two pots of paint
      - instead, inheritance is based on indivisible units that get combined in different ways
      - we now call these “particles” **genes**
    - each individual has two copies of each gene
      - one from each parent
      - some traits are controlled by a single pair of genes
        - Mendel studied these simple cases

- in fact, most characteristics are affected by not just one pair, but many pairs of genes
  - but we will start with simple cases that are only affected by one pair of genes
- the *combination* of the two genes (one from each parent) controls that characteristic
- any given gene comes in two or more variants, called **alleles**
  - so the gene for seed color in peas exists in two alternate forms (alleles):
    - one allele “codes for” yellow
    - the other allele “codes for” green
- **locus:** the “place” in the genetic makeup that holds an allele
  - (plural: **loci**)
  - each individual pea plant has two loci for seed color
  - each of which may contain either the yellow-seed allele or the green-seed allele
- in Mendel’s model, an allele may be **dominant** or **recessive**
  - a dominant allele, if present, determines the characteristic it controls
    - that is, a dominant allele is always **expressed**
    - if the other locus contains a recessive allele, it is masked by the dominant one
  - a recessive allele is expressed only if both of an individual’s loci contain the recessive allele
  - In peas, the yellow-seed allele is dominant
    - Let’s call the dominant “yellow-seed” allele “Y”, and the recessive “green-seed” allele “y”
    - so a plant that has two yellow-seed alleles (YY) has yellow seeds
    - a plant that has one yellow-seed allele and one green-seed allele (Yy, or yY) also has yellow seeds
    - only a plant with two green-seed alleles – the recessive allele – (yy) has green seeds
    - Yy and yY are exactly the same; this just means that one of each allele is present
    - it does not matter which was from the mother or the father
- an individual in which the alleles of a given gene are the same is called **homozygous**
  - an individual may be **homozygous dominant** or **homozygous recessive**
- an individual in which the alleles of a given gene are different is called **heterozygous**
- an individual’s combination of alleles is its **genotype**
  - a pea plant’s genotype for seed color might be YY, or Yy, or yy
- and the observable characteristics that it displays are called its **phenotype**
  - such as having yellow seeds or green seeds
  - in most cases, the phenotype is influenced not only by the genotype, but also by the environment
  - Mendel picked traits that are only minimally influenced by the environment, so the genetic processes are easy to see
- how does this dominant/recessive thing work?
  - in various ways, but one common way is that the two alleles code for two variants of the same protein
  - for example, say that one allele is "normal", in that it codes for a protein that does some function
    - like a protein that is necessary for blood clotting (call this allele C)

- and the other is defective, in that it codes for a slightly different protein that does not to perform the same chemical role
  - the protein produced by the defective allele does not cause blood to clot (call this allele c)
- if an offspring gets two copies of the normal allele (CC), the organism produces the functioning protein
  - and its blood clots normally
- if the offspring gets one copy of the normal allele, and one copy of the defective allele, it still produces some of the functioning protein
  - there may be less of the protein, but in many cases, the function still occurs
  - a heterozygote for the blood clotting allele (Cc) has blood that clots normally
- but if the offspring gets *two* copies of the defective allele, it produces none of the functioning protein; that function then does not occur
  - a homozygote for the defective blood clotting allele (cc) produces no functional blood clotting agent, and his or her blood does not clot
- in this situation, the normal allele is acting dominant, and the defective allele is acting recessive
- this example is the recessive genetic disorder hemophilia
  - which affects only people who get two copies of the recessive hemophilia allele

– actually, there is a third possibility: alleles can be **codominant**
- Mendel did not study any codominant traits, and we won't consider them until later
- but: codominant alleles are those in which a combination of two different alleles produces a trait that is different from that produced by having two of the same alleles
  - such as snapdragon flowers that come in three colors: red, white, and pink
  - these are produced by just two alleles
  - two copies of the redness allele produce a red flower; two copies of the whiteness allele produce a white flower; and one of each produces a pink flower
  - neither is dominant, neither is recessive; they are codominant

– Note that being dominant, recessive, or codominant has NOTHING to do with whether an allele is common or rare
- a dominant allele can be common or rare; a recessive allele can be common or rare

– Also note that being dominant, recessive, or codominant has almost NOTHING to do with whether an allele is advantageous, neutral, or harmful
- a dominant allele can be helpful or harmful; a recessive allele can be helpful or harmful

– Normal cells have two loci for each gene, with one allele at each
- a cell with two loci for each gene is **diploid**

– Parents produce special-purpose sex cells
- sex cells are called **gametes**
  - mother’s gametes (in animals): eggs, ova (ovum, singular)
  - father’s gametes (in animals): sperm
- gametes have only one locus for each gene: they are **haploid**

– Offspring are made by combining one gamete from the mother with one gamete from the father
- the offspring then has two loci for each gene (the offspring is diploid)

    - one locus contains one allele from the mother, and one locus contains one allele from the father
- The concept of **independent assortment:** every allele is equally likely to be transmitted
  - when parents produce gametes, each allele is equally likely to be included in a gamete
    - if a parent has two different alleles (say, Yy), it will produce the same number of Y gametes as y gametes
  - when offspring are formed, each gamete is equally likely to be included in the offspring
    - so the offspring will have a purely random mix of alleles from each parents
    - if we know the parents' genotypes, we can calculate the odds of any given combination of alleles in the offspring
- let's illustrate these ideas with some of Mendel's pea plants
  - background fact: pea plants, like most plants, produce male and female gametes
    - male: pollen
    - female: ovules, located in the base of flowers
  - Say we start with some pea plants that are homozygous
  - in the homozygous yellow-seed plants, both loci contain the dominant allele for yellow seeds
    - we can write this at YY, where the capital letter indicates dominance
      - these plants can only produce "Y" gametes
      - any amount of crossing among them will only produce more "YY" homozygous yellow-seed plants
    - In the green-seed plants, both loci contain the recessive allele for green seeds
      - we can write this as "yy"
      - again, any amount of crossing of these plants will only produce more "yy" homozygous green-seed plants
  - Now, say we cross these two varieties, YY and yy
    - the YY plants produce only Y gametes
    - the yy plants produce only y gametes
    - the offspring that get one gamete from each type of parent (the F_1 generation) all have one gamete from one group, and the other gamete from the other
    - That is, every one of them is heterozygous "Yy" or "yY", which is the same
    - Since the Y (yellow-seed) allele is dominant, all these plants have yellow seeds
    - the visible variation in the phenotypes disappears!
  - Now we cross these heterozygous Yy and yY plants
    - Each of these plants produces a mix of gametes, exactly half with "Y" (yellow-seed) alleles and half with "y" (green-seed) alleles
    - So, when these are combined into offspring (the F_2 generation), each offspring could get either "Y" or "y" from the mother, and either "Y" or "y" from the father
      - There are four possibilities, each equally likely:
        - Y from father, Y from mother: YY
        - Y from father, y from mother: Yy
        - y from father, Y from mother: yY
        - y from father, y from mother: yy

    - three of the four possibilities have at least one dominant Y allele (YY, Yy, and yY)
        - so three out of four members of the F_2 generation have the dominant trait: yellow seeds
    - but one of the four possibilities (yy) has no dominant Y allele.
        - yy individuals have two of the recessive alleles
        - So one in four individuals of the F_2 generation (the “yy”s) has the recessive trait: green seeds
- The model predicts virtually exactly the frequencies of traits that Mendel observed in his experiments with a large number of plants
    - just as you usually have to flip a coin many times before heads and tails start averaging out close to 50-50.
- Another way of looking at this model: the Punnett square
    - Let’s go through the same series of matings
    - with the alleles numbered, so you can keep track of them
        - despite the numbers, all “Y” alleles act the same, regardless of which parent they came from
        - same for all “y” alleles
    - Father is Y_1Y_2 (yellow); Mother is Y_3Y_4 (yellow) (both are homozygous dominant):

	From Y_3Y_4 (yellow) mother: Y_3	From Y_3Y_4 (yellow) mother: Y_4
From Y_1Y_2 (yellow) father: Y_1	Offspring: Y_1Y_3 (yellow)	Offspring: Y_1Y_4 (yellow)
From Y_1Y_2 (yellow) father: Y_2	Offspring: Y_2Y_3 (yellow)	Offspring: Y_2Y_4 (yellow)

    - all the offspring of YY parents are YY.
    - The homozygous recessive parents produce homozygous recessive offspring, too:

	From y_3y_4 (green) mother: y_3	From y_3y_4 (green) mother: y_4
From y_1y_2 (green) father: y_1	Offspring: y_1y_3 (green)	Offspring: y_1y_4 (green)
From y_1y_2 (green) father: y_2	Offspring: y_2y_3 (green)	Offspring: y_2y_4 (green)

    - all the offspring of yy parents are yy, too.
    - Now, what if a YY male (for example) mates with a yy female?

	From y_3y_4 (green) mother: y_3	From y_3y_4 (green) mother: y_4
From Y_1Y_2 (yellow) father: Y_1	Offspring: Y_1y_3 (yellow)	Offspring: Y_1y_4 (yellow)
From Y_1Y_2 (yellow) father: Y_2	Offspring: Y_2y_3 (yellow)	Offspring: Y_2y_4 (yellow)

    - The crossed F_1 offspring are all the same: heterozygotes
    - Since Y (the yellow-seed allele) is dominant, all the offspring express the dominant trait: they all have yellow seeds
    - the colors have not blended. Instead, the green phenotype has completely disappeared.

- If the sex of the parents were reversed (YY mother, yy father), the effect would be exactly the same
- What happens if these heterozygotes mate?

	From Y_3y_4 (yellow) mother: Y_3	From Y_3y_4 (yellow) mother: y_4
From Y_1y_2 (yellow) father: Y_1	Offspring: Y_1Y_3 (yellow)	Offspring: Y_1y_4 (yellow)
From Y_1y_2 (yellow) father: y_2	Offspring: y_2Y_3 (yellow)	Offspring: y_2y_4 (GREEN)

- the original variation reappears!
  - two yellow-seeded parents produced some green-seeded offspring!
  - the green-seed trait was hidden, not expressed, in the parents
  - it only reappeared when an offspring got a combination of alleles that was different from either parent
  - these parents would be called **carriers** of the recessive allele
- There are four possible combinations of alleles here
  - the parents produce each kind of gamete in equal numbers
  - and each gamete is equally likely to be included in an offspring,
  - so if the parents have many offspring, we expect them to produce about equal numbers of each of the four combinations
- three of the combinations produce an offspring with yellow seeds, versus just one combinations with green-seeds
  - so we expect the offspring of these parents to be about ¾ yellow-seeded, and ¼ green-seeded
- this 3/4 to ¼ proportion is exactly what Mendel observed

- Let's exercise these ideas with an example in humans
  - "Hitchhiker's thumb" is a recessive trait
    - in which the first segment of the thumb can bend backwards more than 50 degrees
  - we can call the dominant trait "Straight thumb"
    - we'll call the dominant allele "S" (Straight)
    - we'll call the recessive allele "h" (hitchhiker's)
  - What are the possible genotypes of someone with
    - hitchhiker's thumbs? (hh)
    - straight thumbs? (SS, Sh, hS)
  - How many in this class have hitchhiker's thumbs?
    - notice that a recessive trait is NOT necessarily rare
      - about 25% in the US population have the recessive *trait*
      - of all the *alleles* in the population, about 50% are hitchhiker's, and 50% are straight
    - recessiveness and dominance in themselves do not tell you anything about how common or rare an allele is
  - Can parents who both have hitchhiker's thumbs have a child with straight thumbs?
    - no, because both produce only gametes with h alleles. Neither of them produces any gametes with the S allele.
    - all of their children will be hh, with hitchhiker's thumbs

- If a homozygous straight thumbed woman has children with a man with hitchhiker's thumbs, what fraction of the children are expected to have hitchhiker's thumbs?

	From S_3S_4 mother: S_3	From S_3S_4 mother: S_4
From h_1h_2 father: h_1	Offspring: h_1S_3 (straight)	Offspring: h_1S_4 (straight)
From h_1h_2 father: h_2	Offspring: h_2S_3 (straight)	Offspring: h_2S_4 (straight)

- None; they all get a dominant S allele from the mother, so they all have straight thumbs
- If a heterozygous straight thumbed woman has children with a man with hitchhiker's thumbs, what fraction of the children are expected to have hitchhiker's thumbs?

	From S_3h_4 mother: S_3	From S_3h_4 mother: h_4
From h_1h_2 father: h_1	Offspring: h_1S_3 (straight)	Offspring: h_1h_4 (hitchhiker's)
From h_1h_2 father: h_2	Offspring: h_2S_3 (straight)	Offspring: h_2h_4 (hitchhiker's)

- Half. All the children get one recessive allele from the father; from the mother, half get the dominant Straight allele, and half get the recessive hitchhiker's thumb allele.

- So far, we have only considered a single trait at a time
  - like seed color: yellow or green
  - but what about other traits, like seed shape: wrinkled or smooth?
- Mendel checked to see if the outcome at one pair of loci would affect the outcome at another pair
  - that is, does the process of getting yellow or green seed alleles affect the process of getting wrinkled or smooth seed alleles?
- Result: the alleles at each pair of loci assort independently of every other pair
  - so the offspring effectively get a completely random selection of one of each pair of alleles from each parent
  - this means that offspring will often have combinations of alleles and traits that neither parent had
- Another pea example:
  - Say we start with
    - homozygous yellow, homozygous smooth plants (YYSS)
    - homozygous green, homozygous wrinkled plants (yyss)
    - each can produce only one kind of gamete:
      - YYSS plants produce only YS gametes
      - yyss plants produce only ys gametes
    - if we combine these gametes, the offspring will all be YySs
      - heterozygous yellow, heterozygous smooth
    - now these YySs plants can produce four kinds of gametes
      - YS, yS, Ys, and ys
      - because each gamete gets one of the two color alleles, and one of the two shape alleles

      - each is equally likely, and so is produced in equal numbers
      - when these four kinds of gametes are randomly combined into offspring, all the possible combinations occur in the next generation
        - Overall, they are still ¾ yellow vs. ¼ green
          - and still ¾ smooth vs. ¼ wrinkled
        - But all combinations of color *and* shape alleles are also produced
          - YYSS: Yellow, Smooth…
          - YYsS: Yellow, Smooth… and so on…
          - YYss: Yellow, Wrinkled… a new combination, not seen in any previous generations!
    - We can extend the concept of a Punnett square to cover the combinations of alleles for two genes (four loci) at once
      - another way of writing the same example as above
    - Mendel observed almost exactly the predicted proportions
      - all the possible combinations of multiple loci can be produced
      - how many of each combination are born has nothing to do with how “useful” the phenotype is
        - nor whether that combination was actually present in any parent, grandparent, or other ancestor
        - the odds of any given combination being born results simply from the laws of probability selecting from the mix of alleles in the parents
      - if we consider a large number of pairs of loci, the total number of combinations becomes enormous
        - so we can expect never-before-seen combinations to turn up fairly often

- Obviously, there are many practical and scientific uses for understanding inheritance
  - from plant breeding to modern medicine

- But we are looking at it here because it fills a gap in Darwin’s theory

- What Mendel's theory of inheritance does for Darwin's theory of evolution:
  - Overall, it explains why offspring resemble their parents, yet there is still plenty of variation among individuals
    - from which natural selection can select the ones that leave the most offspring
    - and weed out the rest
  - Specifically:
    - offspring resemble their parents because
      - the parents are the source of the offspring’s alleles
    - variation is not blended away because
      - alleles don’t blend, they just get reshuffled
    - and varying individuals are constantly produced because
      - a vast number of alleles gets completely reshuffled in every generation,
      - creating offspring with an effectively endless variety of combinations of traits every generation