Overview of Lecture: Microevolution I
Read: Text Ch 19

Microevolutionary processes and patterns
Some important examples of contemporary evolution in action.

• evolution of Bacteria on a “Mega-Plate” – evolution in action
• correlated variation in genotypes and phenotypes
• classic Mendelian vs complex quantitative traits
• phenotypic selection within generations
  & genetic response across generations
• genomic approaches –
  SNPs – Single Nucleotide Polymorphisms, and
  GWAS - Genome Wide Association Studies
• phenotypic selection: disruptive, directional & stabilizing
• selection in contemporary humans: Sanjak et al. PNAS
• heritable happiness! (“happiness glasses”?)
• the evolution of cancer & tumors
Learning Goals:

1. Understand and be able to use examples to explain ... What is evolution by natural selection (ENS)? What are the fundamental, necessary and sufficient conditions for ENS? Use examples to illustrate stabilizing, directional and disruptive phenotypic selection.

2. Be able to use the example of the study by J.S. Sanjak et al. PNAS January 2, 2018 to illustrate and explain (a) how patterns of variation in phenotypic traits might be mapped onto patterns of variation in a measure of fitness, (b) how patterns of variation in phenotypic traits might be correlated with patterns of variation in genomic markers (SNPs), and (c) how (a) and (b) can be combined to deduce whether the distribution of some traits that are under phenotypic selection might evolve across generations over time.

3. Be able to use the example of Happiness is in your genes (partly) to explain why showing that a trait has some level of genetic heritability doesn’t imply anything about the potential for beneficial interventions.
https://www.youtube.com/watch?v=plVk4NVIUh8
The Evolution of Bacteria on a “Mega-Plate” Petri Dish (Kishony Lab)
[the original paper in Science is at http://science.sciencemag.org/content/353/6304/1147 ]

What did you learn from this experiment/video?
Making monkeys out of evolutionists

"If evolution occurs, it does so too slowly to be observed. Both theories [creationism, evolution by natural selection] are accepted on faith by those who believe in them. Neither theory can be tested scientifically because neither model can be observed or repeated."

https://www3.beacon-center.org

The BEACON Center for the Study of Evolution in Action is an NSF Science and Technology Center with the mission of harnessing the power of evolution in action to advance science and technology and benefit society.
The 12 Days of Evolution - Complete Series!

Anything helpful, interesting, surprising, puzzling in this?
As a result, the population gradually comes to include more and more individuals with the advantageous characteristics.

Evolution can result from any process [including but not limited to natural selection] that causes a change in the genetic composition of a population.

Note: this implies that not all evolutionary change is adaptive.
Ex: the DNA triplet code is redundant: 4x4x4=64 sequences but only ~23 amino acids. 
Synonymous substitutions at the 3rd position in some DNA triplet codons are “silent,” having no effect on the coded Amino Acid.
Ex: TTT and TTC are redundant, both specify Phenylalanine. Redundant codons can evolve with little or no impact on fitness.
The rate of accumulation of synonymous substitutions serves as a null model for mutation and drift, to compare to selected, non-synonymous substitutions that change AA sequence and protein structure.
An organism exposes its **phenotype** … not its **genotype** to the environment.

**Classical Mendelian traits:**

**Modern genomic perspective:**

**Heritability** is an estimate of the proportion of phenotypic variation in the population.
The top panels show the populations before \textbf{(phenotypic)} selection has occurred … those favored by selection are shown in light brown. The bottom panels indicate what the populations would look like in the next generation. \textit{- if the phenotypic trait “body size” were highly heritable}

- big benthic (shallow w/ plants)
- little limnetic (open water) sticklebacks
Natural selection in humans is happening more than you think

Many [phenotypic] traits like higher body mass index are linked to having more kids [one measure of fitness] and show genetic basis [are at least partially heritable]

Many traits vary among different members of a population … from body size to hair colour, and those differences are often linked to differences in genes.

Natural selection is still influencing the evolution of a wide variety of human traits, from when people start having children to their body mass index, reports a study published Monday in the journal Proceedings of the National Academy of Sciences.

"It's surprising to some scientists. I think it's probably even more surprising to the general public," acknowledges lead author Jaleal Sanjak, who just completed his PhD in evolutionary biology at the University of California Irvine. "It's pretty neat."
Evidence of directional and stabilizing selection in contemporary humans
J.S. Sanjak et al. PNAS January 2, 2018. 115 (1) 151-156;

**Directional selection** results in covariance [\( \sim \) a correlation] between the trait and fitness and can lead to changes in the mean value of a **phenotypic** trait in a population.

Phenotypes may also be subject to **stabilizing selection** or **disruptive selection**, which are both nonlinear forms of selection. The key distinction between stabilizing and disruptive selection is whether the relationship between fitness and a phenotype is concave down or up, respectively. Stabilizing selection … will tend to reduce phenotypic variation while disruptive selection will tend to increase it.
Evidence of directional and stabilizing selection in contemporary humans

J.S. Sanjak et al. PNAS January 2, 2018. 115 (1) 151-156;

Here, we analyze the **phenotypic** and **genetic** correlates of **relative lifetime reproductive success (rLRS)** - the individual lifetime reproductive success divided by the mean [a proxy for fitness] - in the UK Biobank (UKB). The UKB is a large population-based prospective study of the genetic and environmental determinants of aging-related disease. The dataset consists of over 500,000 individuals from the United Kingdom who have been genotyped at common SNPs [what are these?] and clinically phenotyped for many different traits.

We estimate linear (β) [**directional**] and quadratic (γ) [**stabilizing or disruptive**] selection gradients by regressing rLRS onto phenotypes and squared phenotypes.
Evidence of directional and stabilizing selection in contemporary humans
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The observed signals of directional selection are weaker than what has been found in other species. Such statistically significant but weak selection gradients are unlikely to lead to large changes in phenotypic distributions over clinically or socially relevant timescales. But should lead to gradual changes over many generations.

12 traits in females and 14 traits in males have a significant nonlinear selection gradient estimate ($\hat{\gamma}$) - skewed toward negative values corresponding to stabilizing selection.
Evidence of directional and stabilizing selection in contemporary humans
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Just fyi – here are the traits; you don’t need to memorize these things.

**Abbreviated trait descriptions:**
age at menarche (AAM),
age at first birth (AFB),
age at menopause (AMP),
body-fat percentage (BFP),
body-mineral density (BMD),
body-mass index (BMI),
basal metabolic rate (BMR),
birth weight (BW),
diastolic blood pressure (DBP),
educational attainment (EA),
forced expiratory volume (FEV),
fluid intelligence score (FIS),
forced vital capacity (FVC),
hip circumference (HC),
hand grip strength (HGS),
height (HT),
mean time to correctly identify matches (MTM),
neuroticism score (NS),
peak expiratory flow (PEF),
pulse rate (PR),
pulse-wave arterial stiffness index (PWA),
pulse-wave peak-to-peak time (PWP),
pulse-wave reflection index (PWRI),
systolic blood pressure (SBP),
speech reception threshold (SRT) estimate, waist circumference (WC),
waist-to-hip ratio (WHR),
and weight (WT).
Evidence of directional and stabilizing selection in contemporary humans

J.S. Sanjak et al. PNAS January 2, 2018. 115 (1) 151-156;

The phenotypic results are consistent with the action of natural selection, but for adaptation to occur there must be effects on the genetic level. We analyzed genetic data from 157,807 female and 115,902 male unrelated samples. Estimates of the genetic correlations between several traits and rLRS were obtained from the data … [* = statistically significant]

What story does this figure tell?

You can see the data for males in the paper: http://www.pnas.org.proxy2.cl.msu.edu/content/115/1/151.full
Evidence of directional and stabilizing selection in contemporary humans
J.S. Sanjak et al. PNAS January 2, 2018. 115 (1) 151-156;

Here we demonstrate that the genetic variants associated with several traits, [genomic analysis of SNP markers – as with 23andMe or Ancestry.com – some of which are statistically correlated with phenotypic traits] including age at first birth in females and body-mass index in males, are also associated with reproductive success. [directional selection]

In addition, for several traits, we demonstrate that individuals at either extreme of the phenotypic range have reduced fitness — the hallmark of stabilizing selection.

Overall, the data are indicative of a moving optimum model for contemporary evolution of human quantitative traits.

Why “moving-optimum”? How does this relate to directional and stabilizing selection for genetically heritable traits?
Happiness is in your genes (partly)

PNAS First Look Blog Posted on May 29, 2013 by Danielle Venton

… feelings of well-being run in families.

Studies based on surveys of twins and families have estimated ~40% of the variance in happiness (or “subjective well-being” SWB) between people is influenced by genetic factors. (based on phenotypic correlations and kinship as a measure of genetic correlation)

Now, behavioral geneticists, economists and social scientists report …

Meike Bartels and her team examined a pool of about twelve thousand unrelated, fully genotyped people (from the Swedish Twin Registry and the Rotterdam Study). They {found} single nucleotide polymorphisms (SNPs ~”genetic markers”) associated with subjective well-being {SWB = the phenotypic trait}.

They estimated “… heritability” … through a relatively new statistical test: …

~12-18% of SWB variance is associated with additive genetic factors {markers} …

Although our genes play a role in determining our general level of happiness, the team rejects any claim that interventions to increase SWB are useless.

The authors write … “the very same genotype may cause a person to grow to 5 feet or 6 feet tall, depending on nutritional intake.”

In 1979 Arthur Goldberger offered an analogy:

Poor eyesight is largely determined by genetics, but the right set of glasses can restore near 20/20 vision.
The Evolution of Cancer

A cancer cell accumulates mutations, each of which can give the cell a growth advantage over its neighbors. This single cell will divide to populate the tumor until another cell with an even better growth advantage crops up. At that point, the more aggressive cell reproduces rapidly, taking over the tumor. It’s survival of the fittest, with every cell for itself.

But all these cancer-promoting mutations do not occur at once. At each stage, cancer cells face selective pressures that drive their evolution. Cells near the center of a growing tumor face shortages of oxygen and nutrients. And pioneering cells that escape the main tumor must adapt to life in a foreign tissue if they are to establish outposts in other organs of the body. Only those cells that acquire mutations that help them adapt to the changing environment and outcompete their neighbors will survive to divide and conquer.

Although cancer-causing mutations can occur in several kinds of genes, all these mutations ultimately promote cell growth and survival.
Genetic Heterogeneity and Clonal Evolution of Tumor Cells and their Impact on Precision Cancer Medicine

The efficacy of targeted therapies in leukemias and solid tumors depends upon the accurate detection and sustained targeting of initial and evolving driver mutations in cancer cells.

Tumor clonal evolution during cancer progression contributes to the longitudinal variations of clonal, morphological, anatomical, and molecular heterogeneity of tumors.

Moreover, drug-resistant subclones present at initiation of therapy or emerging as a result of targeted therapies represent major challenges for achieving success of personalized therapies in providing meaningful improvement in cancer survival rates.

[Note similarities to the evolution of antibiotic resistance in pathogen populations and pesticide resistance in crop pests]