Evolution of humans & disease

1. Levels of explanation in biology: Proximate vs. Ultimate
If you observe a hummingbird returning to the same bright flower over several days, there are many questions you might ask about what you have seen. What are some of them?

What explains
- Human language?
- Trees being taller than the other organisms they co-exist with?
- Fever?

2a. Mechanisms of microevolution
Mutation

Genetic Drift

Gene flow

Natural (and Sexual) Selection

How important / powerful are each of these four mechanisms?

2b. Adaptive landscapes
- The adaptive landscape is a conceptual framework for evolution—a tool useful in understanding why organisms do not attain globally optimal designs. It can be applied to any characters that evolve—morphology, physiology, behavior, etc.
- The adaptive landscape is the surface that describes that subset of design space that is physically, chemically, and biologically possible, given a particular environment.
- Imagine a sheet of ice on a pond. Air bubbles rise to the high spots on the underside of this piece of ice, and roll up from the low spots.
- Bubbles : particular populations/individuals in the design space of the sheet of ice
- Height of the peak : how adaptive that morph is
- Depth of the valley : how difficult it is to go between peaks, e.g. from a locally high peak (somewhat adaptive) to a globally high peak (optimal)
- Force of gravity (pushes bubbles up by driving water down): natural selection
- The likelihood that a morph that is locally well-adapted can become a morph that is globally well-adapted (move between peaks) is not affected by the difference in relative height between those peaks, but on the depth of the valley separating them.
- Natural selection cannot move morphs down from a high point. It therefore cannot be solely responsible for a move from a peak to another peak. Morphs must move by some non-adaptive process to a valley, at which point natural selection can kick in again and move the morph up another peak.
- From a peak, a move in any direction is less adapted than the current condition.
- Changing environmental conditions can convert a peak into a valley.
- Original ref: Wright, S. 1932. The roles of mutation, inbreeding, crossbreeding and selection in evolution. Proceedings of the Sixth International Congress of Genetics 1:356-366.

2c. Historical constraint: you can't get there from here

- *Also called **phylogenetic constraint.***
- In addition to the four mechanisms of microevolution, the phenotypes of individuals, and therefore of entire lineages, are determined by ***historical constraint***: Because of the long evolutionary history of a lineage, an organism's current form may not immediately (or possibly ever) be transferable into a different form.
- There may be a "better" (more efficient) way to do something, but no way for selection to act on it to get it there (due, perhaps, to issues raised by the adaptive landscape model).

Examples of historical constraint:
The vertebrate eye

Wings in flightless birds

2d. Arms races & the Red Queen

- In Lewis Carroll's *Through the Looking Glass*, the Red Queen tells Alice: "It takes all the running you can do, to keep in the same place."
- The Red Queen has since been co-opted as evolutionary shorthand for interactions between any two evolving, and responsive, players: e.g. predator and prey, or host and disease.
- Any co-evolved relationship which incurs costs to both sides will result in a struggle for survival and/or reproduction. That is, both players need to be constantly running (adapting, changing their responses on the playing field) because the landscape in which they exist is constantly changing.

2e. Mimetic evolution

- Darwin (and Wallace) elucidated genetic evolution (change in frequency of genes), although it would be many years before Mendel helped elucidate the particulate nature of inheritance.
- One of Darwin's important innovations was to refute Lamarck, who argued that traits acquired during an individual's lifetime can be passed on to offspring. E.g.: a short-necked giraffe living in a landscape of tall trees might stretch its neck, and that longer neck could be passed onto the giraffe's children.
- However: Lamarckian evolution does occur in one important realm: cultural evolution. Just as genes evolve, so do memes, and they change not just at the boundaries between generations, but also within individual lifespans.
- Meme: a unit of cultural transmission, or a unit of imitation. Examples: tunes, ideas, catch-phrases, fashions, ways of making pots or of building arches. (Dawkins, 1976).
- Memes propagate themselves in the "meme pool" by leaping from brain to brain (as genes propagate themselves in the gene pool via eggs and sperm).
- Like genes, memes are subject to the same mechanisms of microevolution as are genes and the heritable traits they code for.

A false dichotomy: Nature vs. nurture

- Genes ("nature") evolve. Genes code for proteins that comprise many aspects of phenotype, including behaviors.

- The environment (“nurture”) of an individual includes other conspecifics (offspring, potential mates, neighbors, which have also evolved—nature or nurture?), heterospecifics (predators, competitors, symbionts, diet, diseases—nature or nurture?), and abiotic conditions (climate, geography—nature or nurture?).
- But: culture also evolves. Nature or nurture? Culture (across many species) comprises suites of individual and population-level behaviors and expectations about future behavior.
- Furthermore, the “environment” of a single gene includes neighboring genes, which directly affect the expression of the first; if even gene expression is affected by environment, in what context can we expect the question “Nature or nurture?” to ever make sense?

2f. The Naturalistic Fallacy

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2g. Another fallacy: Group selection

- *Individuals* (trout, mayflies, zooplankton, cedars…) are selected to maximize genetic reproduction over their lifetime. Those genes that are passed on to the next generation in the greatest numbers are, by definition, the most successful. Individuals who do not reproduce are not (genetically) represented in the next generation. (However, to the extent that an individual’s kin (siblings, cousins, etc.) share his genes, he has a genetic interest in them being (reproductively) successful.)
- Organisms do not behave so as to benefit the species. There is no heritable mechanism whereby “species level selection,” or “group selection,” could occur (but cultural evolution can and does operate at the group level). If important concepts aren’t being passed between group members, there’s no reason to believe that the entire species should benefit when one individual does. In fact, usually it is just the opposite: in a landscape with limiting resources, more unrelated individuals seeking exactly the same thing (food, mates, territories) puts more burden on each individual.

Thus: Social Darwinism ≠Darwinism

- ***Social Darwinism*** (aka eugenics): this ideology from the 1870’s misapplied Darwin’s tenets to conservative political conclusions. It argues that those members of society who are rich and powerful are therefore the fittest, and thus entitled to all that they have, and more. Thus, as a society who cares about its future, we ought to protect and help those who are already winning the races of resource accrual and social preeminence. Those who are "winning," by modern standards, must therefore be more fit, and thus favored by evolution.

- The 3rd Reich took this further by arguing that we ought concern ourselves with species purity, selecting those individuals for future representation in the gene pool who met Hitler's exacting standards.
- ***Darwinism*** does not make assessments about the good of the species (or the race). Understanding the evolutionary bases for diseases in humans may aid us in formulating savvy health care practices and public health policy—all in service to the health of individual people, ***not*** to fashion a population that looks a particular way.

3. What makes us human?

4. How have our lives changed from the conditions in which we evolved?

- Hominid lineage split from other apes (5+ mya)
- Anatomically modern humans (≈ 100,000 ya). (Hunter-gatherers in fission-fusion groups in savannah or open woodland habitats.)
- Agriculture (≈10,000 ya)
- Cities (≈9,000 ya; Jericho, pop 3,000; ≈6,000 ya, Mesopotamian cities of ≈25,000)
- Industrial revolution (≈late 18th century)
- Modern conveniences (e.g. electric light, corrective lenses, central heat, internal combustion engine, air travel, telephones, computers, antibiotics…)

What are the likely evolutionary and health effects of these transformations?

Basic premises of Darwinian medicine (aka evolutionary medicine)

- Before acting to "correct" a health issue (e.g. fever), consider why we are experiencing it in the first place (that is: ask what its *ultimate* explanation is). Evolution is powerful (but not omnipotent)—if there were no adaptive advantage, there is a significant chance that the "problem" is adaptive.
- Or: there is a good chance that the "problem" ***was*** adaptive, under pre-modern conditions. As living conditions in modern societies continue to diverge from those under which we experienced most of our evolutionary history, that "biological legacy" potentially predisposes us to a variety of both infectious and non-infectious diseases.

4. Darwin's Hostile Forces are pressures that cause differential survival and reproduction, which all living organisms must respond to successfully (if they are to survive and reproduce). These include:
–Climate
–Weather
–Food shortages
–Predators
–Inter-specific competition
–Intra-specific competition
–Pathogens (disease and parasites)

Strategies for dealing with each of these "hostile forces" differ. For instance: responses to regular, predictable, abiotic forces (e.g. Winter) should be relatively easy to evolve. Responses to biotic forces will result in arms races, however. For humans, who are our competitors?

The most hostile forces for humans are…

The evolution of virulence (Definition: the capacity of a pathogen to invade host tissue and reproduce; the degree of pathogenicity).

- A pathogen with very high virulence will kill its host quickly, before it has a chance to spread to other hosts; this would comprise an evolutionary dead-end for that pathogen. Very low virulence may allow for the longest window of opportunity of spread to additional hosts, but if the host is not "acting sick," there may be no method of transmission (e.g. if spread is through respiratory droplets).
- Mode of transmission may predict optimal degree of virulence for a particular pathogen: consider the often long latency between HIV-infection and AIDS.

What causes disease and other health problems? We now have several tools with which to address this question:

- Proximate explanations are likely to address symptoms only, or fail to recognize adaptive responses of the body as such.
- The Red Queen lives—host and pathogen are constantly evolving new strategies in response to one another.
- Thus, the adaptive landscape on which we exist is constantly shifting, as the environment in which a particular adaptive response exists is shifting with the arms race.
- Thus: what was selected for (and thus adaptive) 5 mya may now be a liability (e.g. fat and sugar are delicious). On the other hand, what appears to be a liability today may still be an adaptive response.
- Modern living conditions may give pathogens (and non-infectious disease) an advantage in the arms race, if, for instance, density-dependence is a characteristic of a disease's epidemiology.
- Inherent trade-offs in all systems (evolved or designed) means that there will always be design compromises in humans (and other organisms). For instance: walking upright allows us to carry things (food, babies), but predisposes us to lower back

problems. A medical complaint of lower back pain may simply focus on the cost of bipedalism, without recognizing the many benefits of having our hands free.
- Historical constraint means that we are living with evolutionary legacies which selection cannot act upon, due to the nature of adaptive landscapes. For instance: the inefficient and dangerous arrangement of the trachea and esophagus.

Defenses vs. Defects
- Severe pneumonia causes, in fair-skinned people, darkening of the skin and a deep cough. Why?
- Skin pigmentation: defect. Hemoglobin is darker in color when it lacks oxygen, so darker skin is an indication of another problem. Correct the defect--turn the skin pink again--and the result will be beneficial.
- Cough: defense. The cough of pneumonia is the result of a complex mechanism designed to expel foreign material into the digestive tract, where it can be expelled or swallowed (and then destroyed by stomach acid). Thus the cough is not the problem, but a protective response to the problem. Eliminate this defense (block the cough), and you may die of pneumonia. (source: Nesse & Williams, 1994. Why We Get Sick.)
- However, since many pathogens spread through respiratory contact, a cough can also be a mode of transmission, and thus a public health concern.

6. And finally: What are the prerequisites for the start of a pandemic?
   1. A novel virus subtype must emerge to which the general population will have little or no immunity
   2. The new virus must be able to replicate in humans and cause serious illness.
   3. The new virus must be efficiently transmitted from one human to another.

As of May 2005, so-called "avian influenza" (aka avian flu) met the first two prerequisites (Alvarado de la Barrera & Reyes-Teran. 2005. Influenza: Forecast for a Pandemic. Archives of Medical Research 36(2005): 628-636.)

As of January 2006, the Turkish avian flu strain has 3 unique mutations, two of which could make the virus better adapted for humans (either poultry-human or human-human transmission).
- Mutation 1: substitution of an amino acid at position 223 of the haemoagglutinin receptor protein, which allows the flu virus to bind to the receptors on the surface of its host's cells. The mutation increases the virus's ability to bind to human receptors, decreases its affinity for poultry receptors; and encourages the virus to target receptors in the nose and throat.
- Mutation 2: a substitution of glutamic acid with lysine at position 627 of the polymerase protein. This mutation is one of ten genetic changes that gave rise to the 1918 pandemic flu virus. Glutamic acid is associated with flu-virus replication in birds, while lysine is associated with replication in primates. This mutation also helps the virus survive in the cool nasal regions of the respiratory tract.
- In humans, the virus is more likely to spread through droplets coughed from the nose and throat than from deeper (e.g. lung-based) infections, which both of these mutations facilitate. (Source: Butler, D. 2006. Alarms ring over bird flu mutations (News). *Nature* 439, 248-249.)