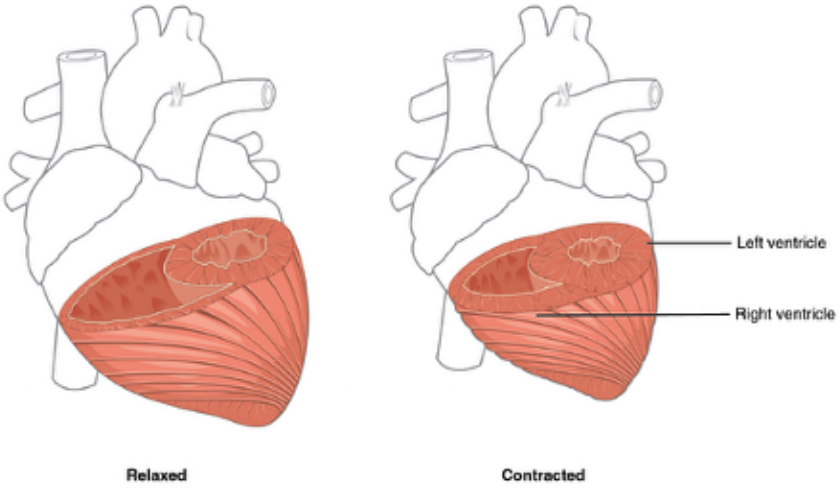
BS1016: Physiology
Heart

Path Dependence
A trait ⇒ usually arises from a certain condition, **de novo**, modify and descent with modification. **Not something new entirely**

Homology
Same ancestor, phenotype related

Convergence
Two different ancestors, trait become similar

Divergence
Same ancestor, trait becomes different



Pulmonary Loop ⇒ is shorter (to lungs)
Systemic Loop ⇒ is longer (to entire body)
The longer the loop, the more resistance
To maintain the same kind of current, **you need more pressure**

The harder it works, **the muscle gets micro tears ⇒ it gets repaired**
Greater thickness of the muscle

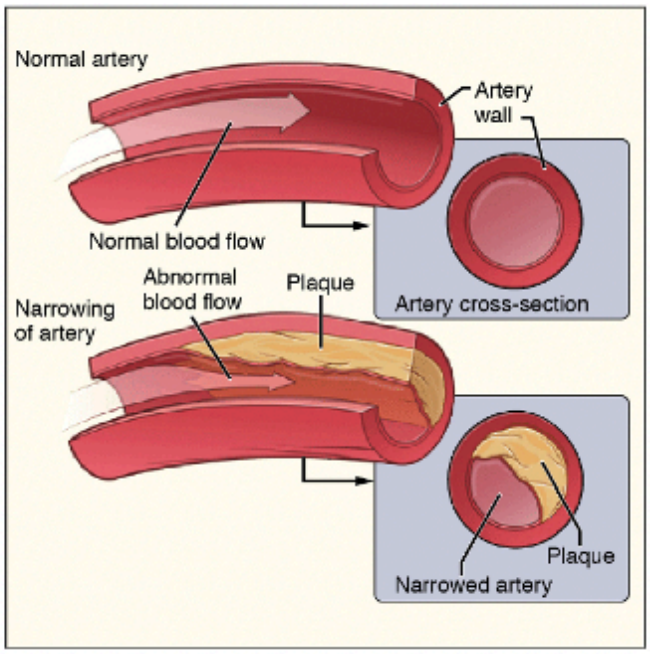
Law of Laplace ⇒ Inside is inversely proportional is to the thickness of the wall

Stress → immune regulation, **faster process of plaque function**

As it is shorten, **the resistance increases**

These blood vessels are **compliance**

1. Systole → diameter increase, they're flexible
2. Diastole → goes down
3. The heart **works easier** by modifying **blood vessel radius**.
4. When plaques form, **the tissue is more fibrous ⇒ compliance drops, radius can't be used as a mitigating method.**
5. To maintain the same pressure, **the heart needs to work harder** (because the radius helps).
6. It then **causes the heart to experience hypertrophy**

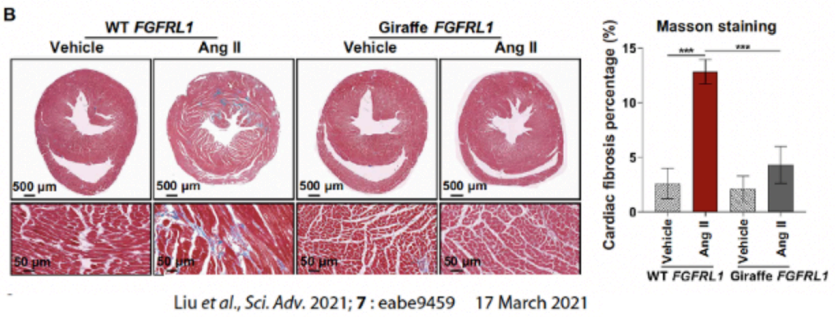


Big Hearts of Giraffe

Giraffes are the tallest animals on the land, their head towering up to six meters from the ground. Their closest relatives are okapi, who has normal neck. Cervical elongation in giraffes occurs as they diverged from okapi around 10 million years ago.

Giraffe heart must pump blood across the gravity to its head, at a pressure that is nearly double that is required for human heart. In keeping with high pressure requirements, the left ventricular wall of its heart is ginormous, and lumen of the ventricle is comparative small. If humans had that degree of ventricular hypertrophy, they would soon drop dead of heart failure (and presumably so will okapi). One of the main reason ventricular hypertrophies causes heart failure is fibrosis, whereby thicker walls with excessive deposition of extracellular matrix becomes stiff and hence cannot pump the blood efficiently.

FGFR (fibroblast growth factors receptors) bind to fibroblast growth factors to initiate a variety of cell signaling pathways. These receptors have wide ranging effects during tissue differentiation, mainly around increase in mitosis. When scientists compared genomes of okapi and giraffes, they discovered that genes for one of the FGFR have seven nonsynonymous mutations in the part that binds to the ligand. Scientists took out the giraffe version of FGFR and inserted it in mice. They then infused mice for four weeks with angiotensin, a kidney hormone that increases blood pressure. Here is what they observed: mice with giraffe version of FGFRL1 shows less fibrosis even as ventricular walls thickened due to hypertension.



Liu *et al.*, *Sci. Adv.* 2021; **7** : eabe9459 17 March 2021

Do you think FGFRL1 gene in giraffes has gone through natural selection?

Vehicle is control

It's not about Lamarck's theory ⇒ Why heart failure?
Many die because of heart hypertrophy

Any giraffe that **doesn't have bigger heart walls are already dead**. True.
What if the mutation came first?

a. Doesn't mean that it went through natural selection
b. If it's naturally selected ⇒ why don't we have it?

WT ⇒ Wild Type
Hypertension is through **Angiotensin II**

a. The hypertension shows **fibrosis**. As the liquid comes into a sphere at high pressure, it creates damage. Microdamages happen as far as capacity of repair + repair is balanced → **Healthy Hypertrophy**.
b. When scar → less pliant. Repair is done **on an emergency** basis, lots of collagen and things. **The damage overshoots capacity of repair ⇒ fibrosis**.
c. The heart is **going through allostasis** → less pliant, **doesn't contract nicely**.
d. It can't expand completely/inject completely
e. Any increase in turn blood pressure ⇒ heart muscle hypertrophy
f. In Wild Type ⇒ Hypertrophy is Fibrosis
g. In Giraffe Type ⇒ Hypertrophy goes smoothly.

How to know?

a. Take a piece of DNA + a DNA from a phylogeny cousin.
b. Differences? **Maybe gene drift**.
c. If it's one particular allele, **linked to physical things around it**. **The further apart, the lesser probability of mixed**.
d. The ones nearby are taken **also (selective sweep)**.
e. See the ones nearby ⇒ **take, start taking in ectopic manner (out of the context)**
f. Approach ⇒ **phylogenetic comparison**, check selective sweeps, do educated guests, take expressions → **see results**

Divergence ⇒ Start with an ancestor.

1. Change the environmental condition
2. Some goes to A, some goes to B trait.

Everytime you have physiological change ⇒ so many genes need to be changed
Giraffe → **change the heart, change the neck**

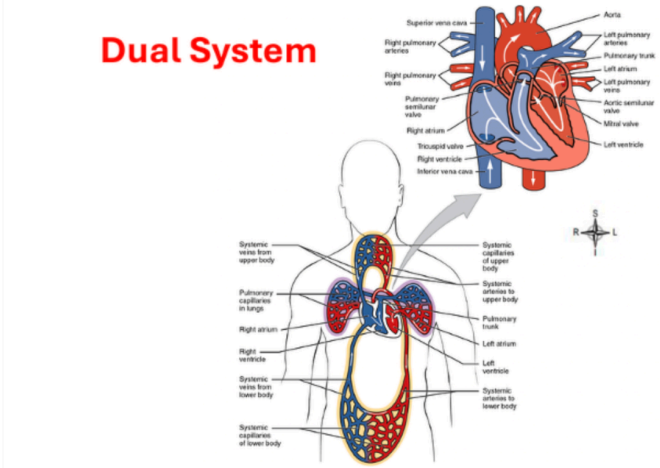
a. A strong heart doesn't mean anything
b. A long neck doesn't work without a strong heart

All must occur together. **Either all works, or nothing works**

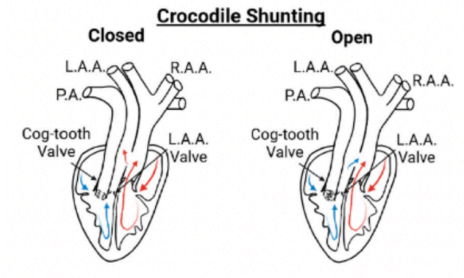
Variations come randomly ⇒ **how do these two happen simultaneously**?

Heart of a Croc

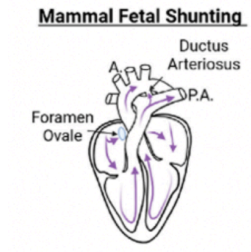
Crocodiles have a four-chambered heart (unlike most of reptiles and more like mammals). A four-chambered heart provides good separation for pulmonary and systemic circulation, which is good because smaller length of vessels going to nearby lungs have lesser resistance and hence need less pressure. We went through this in the lecture:



Crocodiles also have a habit of diving for long time, during which lungs are not really doing their normal business of gas exchange. So, all that pulmonary circulation served no purpose. So, their heart does something cool. It has a shunt that can close blood path going from right ventricle to pulmonary arteries and instead open an alternative path directly to left ventricle (from where blood can access systemic arteries).



Human fetus also has a shunting mechanism. There is a hole that allows blood from right atrium to flow to left atrium, foramen ovale. As the newborn takes its first breath, lungs open up, leading to blood rushing to left atrium. The pressure in left atrium becomes larger than right atrium; it causes the flap-like tissue of foramen ovale to close. It is then sealed in most of individuals by one month of age.



Do you think these two shunts in crocodiles and humans evolved from a common ancestor? Or do you have an alternative explanation?

Homology ⇒ Common Ancestor, same structure possibly different function
Bats and Humans (limb structure)
Convergence ⇒ Different Ancestor, different structure possible same function
Bats and Birds (wings)
Or Stochastic? (random)

Occum's Razor ⇒ explanation with the least assumption

Homology

Common ancestor → became

a. Bird (4 chambered hearts)
b. Reptiles (5 chamber hearts) ⇒ some have 2 lateral ventricles, while the crocodile **has 4 chambers.** Other reptiles **doesn't have a perfect septum**
c. Mammals (4 chambered hearts) ⇒ shunt in fetal stage on atrium side

Stochastic

If something happening by drift is B ⇒ then happening twice is B squared

Sudden Infant Death Syndrome (SIDS)

3 same events happening, all independent is **extremely rare** ⇒ too many assumption

Less likely to happen

Convergence

Looks like the most possible explanation

Two different answers to the same problem.

a. One is from a reptilian
b. One is from a pre-mammalian

The design principle is different.

Crocodile Heart is **Divergent** of the Reptilian Heart, while **Convergent** to the Human Heart.

Pandas

a. They're a bear, all their paws are fused
b. How does one get **a panda to eat bamboo and hold it? ⇒ they have 6th finger, almost like a thumb**
c. It's a divergent evolution, **important to hold things**.

How do you get evolution in multiple things together?

Convergent ⇒ **variation almost always is present**

Can be multiple ways (stabilizing selection).

It tells you that when you go back to the start of everything →

It always reaches the same place. Sequence of variation is less important, because that variation has always existed

Directional Pressure

Amino Acids, Codons, DNA machineries ⇒ there's almost no variation

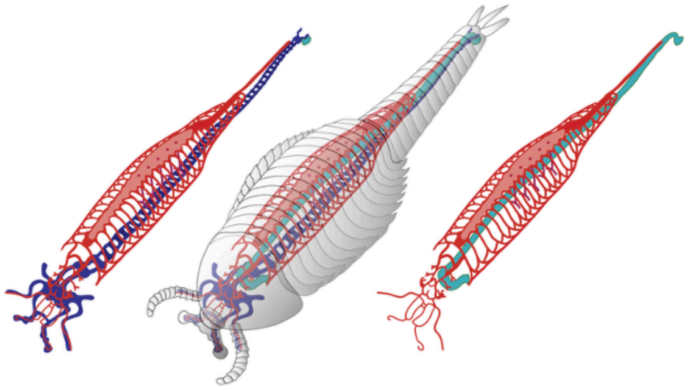
If you don't do it, you're dead. **Any other way, there's no underlying variation**

All variations are gone.

Why the next long? Heart strong?
That variation is present in everyone (some form).
Some people lose their ability to digest lactase as they grow old, **while some continue to be able to** all throughout their life.

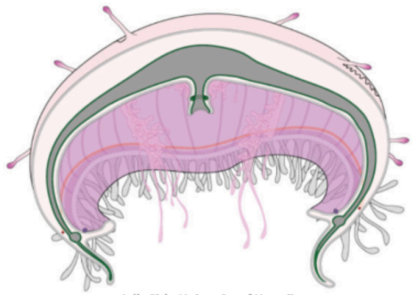
Neck and the heart ⇒ **co-evolution**
One is selecting pressure on the other. **Both are just moving on top of each other**. Mutualistic association to one another.

In 2013, a bunch of scientists discovered a very well-preserved fossil of an early arthropod who lived 520 million years ago in what is now Yunnan province in China. The fossil was indeed so exceptionally preserved that scientists were able to recreate its circulatory system. See below. I will talk to the class about how this system worked based on what we know about current arthropods.



NATURE COMMUNICATIONS | 5:3560 | DOI: 10.1038/ncomms4560 | www.nature.com/naturecommunications

In contrast, below is a rather basic version of circulatory system in a jelly fish, a cnidarian.



Jelly Fish; University of Hawaii

Asking you an easy question. Tell me what would happen if a jelly fish grew a big and as thick as an arthropod?

Building a house

You can build a wall first, and then roof.

Each time replay, **different outcomes**

But **giraffe neck ⇒ When something comes, I keep it. Wait for another. Almost like a deliberate design from the start**

→ the argument **is 100% faulty**

Crayfish

The heart is neurogenic ⇒ ostia (holes)

a. The muscles will contract/relax depending on neuron activity.
b. The whole thing is suspended on the body wall with skeletal muscles.
c. Make sure the flow of the liquid is unidirectional ⇒ ostia → terminal
d. **There's no closed system**. Diffusion won't do the trick ⇒ **convection** distributes nutrients and oxygen.
e. Using **closed loop ⇒ can be controlled with vasoconstriction/dilatation**. You can't choose where it goes, or use a hormone and **send it somewhere**.

f. The brain needs more glucose → to create **sinus**, inside a closed space put blood vessels. **A smaller pot, similar to a closed system**. Local adaptations, but not most of it. They have physical limits on how complicated body plans can be.

Jellyfish

a. No polarization → no brain.
b. One cavity, **mouth and anus are the same**.
c. No Circulatory System.
d. As long as the cell remains one layer and thin, **it can go as big as you want**. There's no reason for it to thicken ⇒ **if thick, cannot diffuse well**
e. It cannot differentiate into tissues. Most jellyfish are dead (jelly). There is a sandwich of the cells, one cell thick.
f. Once they are piled on top of another ⇒ **limits of diffusion are exponential**. There is a physical limit on the type of tissue and amount it can make. **All are one cell thick.**

Color of skin when it shifts ⇒ changes quickly

a. If the mutation **had to arrive every time → very difficult**
b. They can't just disappear, reappear. Biological Variations **happen in sequence in a random manner**. The skin is **not directional, it's stabilizing selection**.
c. It can change. Almost all things in Biology is a stabilizing selection.

Law of Independent Probability ⇒ hard to imagine

Write what we've discussed. Exam cases won't be as difficult, more context and smaller. Practice,write, rewrite, and figure out how it is.

See graph ⇒ middle part
See the contents → recreate the phenotype
If it makes sense, **that's the locus of the evolution**