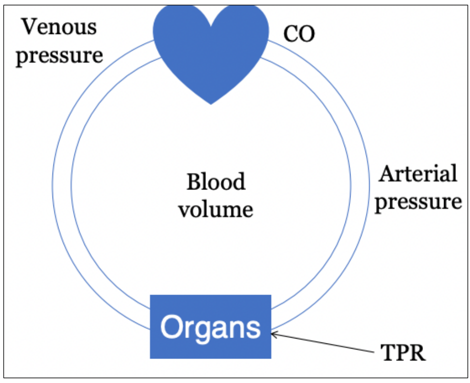
PHYS30012 Complete W1-12 notes (H1)

<u>**W1 vid2 – Normal Cardiorespiratory Reflexes**</u>



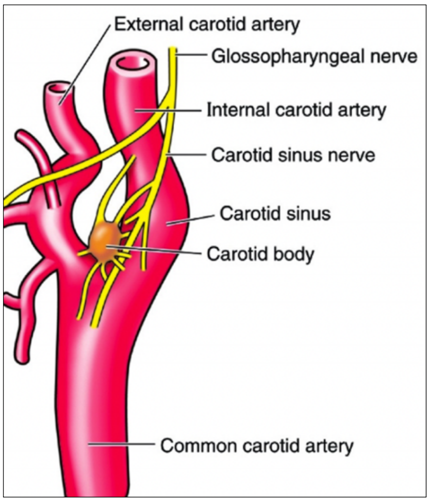
Intro

- Pic - The **cardiovascular (CV) system framework:**
- **The *primary* purpose of the circulation is to provide adequate blood flow to the organs**
- **Autonomic control of the CV system** determines the optimal **cardiac output** and its distribution to our organs to meet the **metabolic demands.**
- **Can the body measure cardiac output directly? No** – because there's no means of measuring flow, but we can measure pressure which is used as a surrogate because CO is related to BP. Higher CO = higher MAP. It takes advantage of the basic baroreflex.
- **Basic baroreflex:**
  - <u>Increased arterial pressure</u> -> <u>Increased baroreceptor discharge</u> -> Central neural processing -> Vasodilation, reduced CO -> Arterial pressure returns to normal.
  - It's a negative feedback reflex – whereby if you increase pressure, you then reduce it. Steps in b/w involve sensors + sending info to brain + messages from brain to heart, etc.
- **Can the body measure pO2 directly? Yes**. To maintain pO2 the body uses the basic chemoreflex vv
- **Basic chemoreflex:**
  - <u>Reduced arterial pO2</u> -> <u>Increased chemoreceptor discharge</u> -> Central neural processing -> Increased ventilation (more O2) -> Bradycardia, vasoconstriction (less O2 use) -> Arterial pO2 returns to normal.
    - Note: bradycardia = slower HR. And this means less O2 is used around body.
    - Vasoconstriction also allows less O2 use. But brain is excluded from vasoconstriction.
  - It's called 'basic' chemoreflex bc it's chemoreflex measured in isolation + without input from organs (in particular lung movement).

Sensor location

- **Sensors**
  - <u>Mechanical sensors</u> (mechanoreceptors) = sensors for **pressure**.
  - <u>Biochemical metabolic sensors</u> – detect **pH + pO2**.
  - From the sensors, info is sent to brain via <u>afferent neurons</u> – these neurons relay information to control centres in the CNS.
- **Where is the major group of sensors for arterial pressure? carotid artery**
- **Where is the major group of sensors for pO2? Carotid artery**

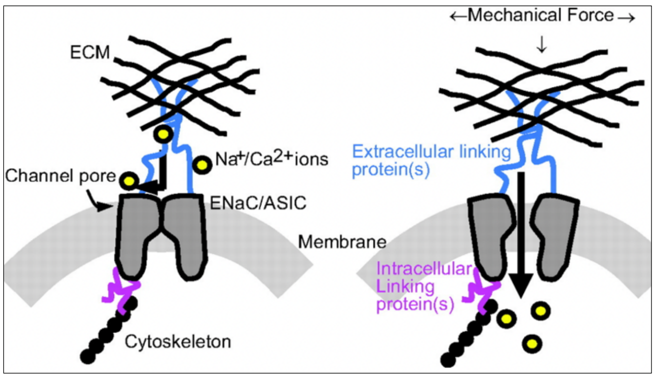
- **Major CV sensors**



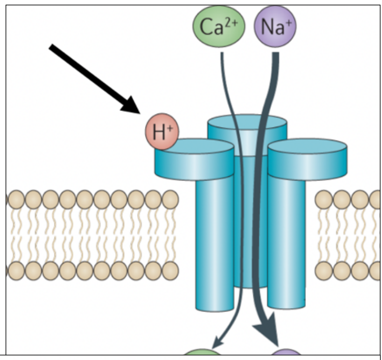
  - Pic shows common carotid artery coming up from the aortic arch. It divides into the internal carotid artery (which supplies blood to brain) + external carotid artery (supplies blood to superficial structures in head).
  - Brain is most imp organ in body. If you want to make sure that brain is receiving adequate flow w/ adequate metabolites (as measured through O2 levels) – then the most imp place for **sensors is in internal carotid artery** – and that's where they are.
  - For **arterial pressure – baroreceptors are in the carotid sinus**.
    - The artery wall thins around this location. Since it's more thin, it's more compliant and able to respond to small changes in pressure.
    - **Small change in pressure = causes change in stretch of artery wall** – and this is picked up by baroreceptors.
    - Baroreceptor operating range: 40-200 mmHg. So they can detect pressures over this range.
  - For **detection of pH + pO2 in blood – there are set of chemosensors located in the carotid body**.
    - Carotid body sits outside the internal carotid artery.
  - Both sensors ^^ are in:
    - Strategic locations (to make sure that particularly brain maintains stable blood flow + O2).
    - Have perfect structure (particularly the carotid sinus with redesigning of artery wall to make it more sensitive).
  - Messages from carotid sinus + carotid body to brain travel up via carotid sinus nerve, and then via glossopharyngeal nerve and then up to brain.

Sensor biology

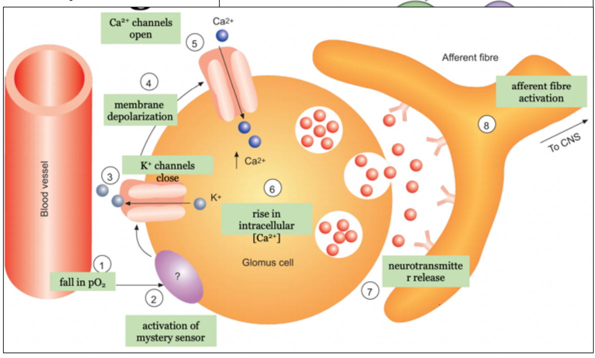
- **Mechanoreceptors are usually transmembrane proteins**
- **pH sensors (a metabolic receptor) are usually transmembrane proteins**
- **DEG/ENaC ion channel family**
  - This is one major family in the world of mechano- and pH receptors.
    - It's a transmembrane protein. A large external component of the protein is extracellular.
    - Cartoon depiction on slide 19.
  - **ENaC** = epithelial sodium channels.
    - These are all mechanosensors.
  - **ASIC** = acid sensing ion channels.
    - ASIC2 is a mechanosensor. ASIC1 and ASIC3 are acid sensors.
- **Mechano-transduction – ENaC + ASIC**
  - 2 subunits. Extracellular portion of protein is linked in with the extracellular matrix.
  - There are Na and Ca ions in ECF.



- When **mechanical force stretches ECM**, it's detected by the transmembrane protein – which changes the shape of the pore to allow Na + Ca ions inside the cell.
  - The ions coming inside the cell act as a signal of stretch.

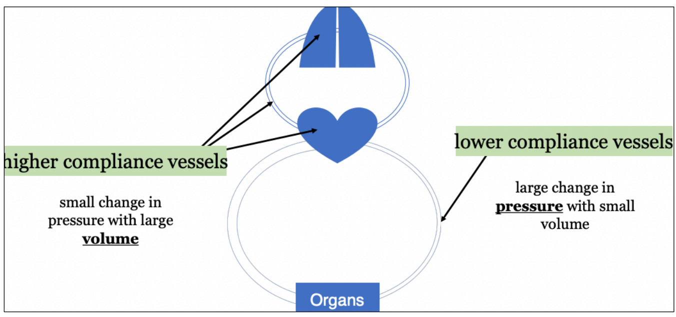


- **pH sensing - ASIC**
  - There are Na and Ca ions in ECF.
  - **H+ comes** to a portion of the extracellular portion of the transmembrane protein. This then triggers a change in protein conformation to open the pore and allow Na + Ca ions inside the cell.
    - Again, the ions coming in is detected as a change in pH.
- **O2 sensing – K+ channels**
  - Pic shows glomus cell. Glomus cells are found in carotid body and other chemoreceptors around body.



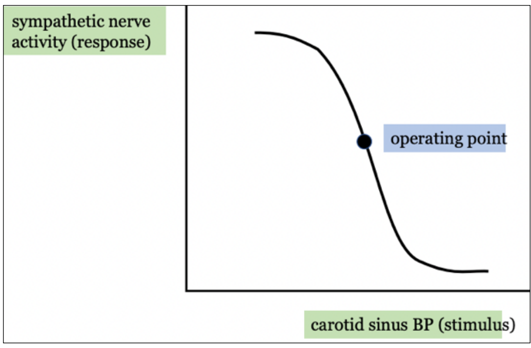
  - **Steps**:
    - 1. Blood vessels are next to glomus cells, and as blood is flowing past – if there's a **drop in pO2** – this activates a mystery sensor in the glomus cell.
    - 2. The sensor changes K+ movement through K+ channels – it causes K+ channels to close. So there's more K+ inside, and cell membrane depolarises.
    - 3. Depolarisation causes conformational change of Ca2+ channels – causes Ca2+ channels to open and allow Ca into cell.
    - 4. Rise in intracellular Ca causes a series of changes which result in fusion of vesicles with cell membrane – and neurotransmitters are released.
    - 5. The neurotransmitters stimulate receptors on afferent fibres, which send messages up to brain.
  - Recall basic chemoreflex = drop in pO2 = afferent nerve stimulation.
    - Note: pO2 = partial pressure of O2.
- **Glomus cell neurotransmitter(s) include……**
  - **1. noradrenaline**
  - **2. dopamine**
  - **3. adenosine**
  - **4. acetylcholine**
  - **5. ATP**
  - **6. substance P**
  - **7. met-enkephalin**

Sensor physiology



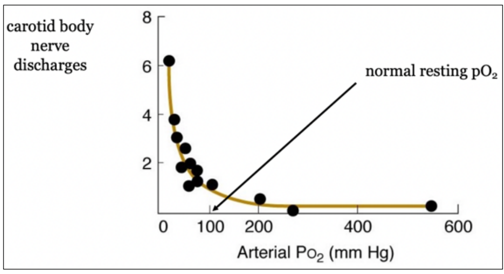
- **Mechanoreceptors**
  - Mechanoreceptor info depends on if they are in high compliance vessels or heart chambers – e.g. atrium, pulmonary artery, lungs.
  - In **higher compliance vessels** -> we see **small change in pressure** with **large volume** change.
    - So stretch (detected by mechanoreceptor) will tell about volume c.f. pressure.

- In **lower compliance vessels** -> we see **large change in __pressure__** with **small volume** change.
  - So stretch (detected by mechanoreceptor) will tell about pressure changes c.f. volume changes.
- **Carotid sinus mechanoreceptors (baroreceptors)**
  - They are stimulated by __increasing stretch__.
    - Response of CV reflex = bradycardia (slow HR) + lower BP (via vasodilation).
  - Stretch reflects __pressure__.
    - Discharge rate is proportional to blood pressure. So more discharge during systole.
  - They __respond quickly__ to changes in pressure.
  - They are __sensitive__ (aka sensitive to small pressure changes).
  - **Arterial baroreflex**
    - Buffers day-to-day threats to stable BP – these threats that can increase BP include:
      - Eating.
      - Talking.
      - Anxiety.
      - Defecation.
    - Baroreflex prevents such ^^ rises in BP from going too high. It's also involved in making sure BP doesn't fall too much either.
    - Aka BP range is small – not much variability.
      - Loss of carotid body / baroreflex = greater variability in MAP (experience higher + lower BPs).
    - At night, the average BP is less.
- **Baroreflex stimulus-response curve** – this curve describes the way the system works.
  - __Stimulus__ = BP in carotid sinus. __Response__ = SNS activity.
  - It's a __sigmoid__ curve and it works around an operating point of BP that the body likes to maintain.
    - Note: the curve is __steep in the middle__ – indicates that it's very __sensitive__ to small changes in BP.
      - This isn't true at very low or very high BP levels. This may be because the threshold of response is reached so either baroreceptors aren't firing or can't fire any more (so SNS nerve activity remains stable despite BP change).



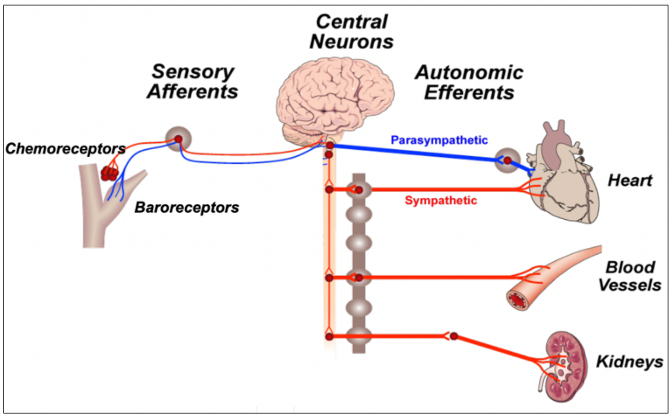
  - So if BP increases (move right on x-axis) – then we move down the curve – aka SNS activity decreases.
    - Conversely – if BP decreases, SNS activity increases.
  - ^^This is to make BP go back to normal.
- **Carotid body chemoreceptors**
  - **Stimulated** by __falling pO2, falling pH or rising pCO2.__
  - **Response** = __increased breathing + tachycardia__* (increase HR) + __higher BP__ (bc of vasoconstriction).
    - *tachycardia represents the influence of increased lung stretch in the integrated response.

- Note: in basic chemoreflex we saw bradycardia (in isolation). But in intact organism we see tachycardia. This is bc there's a reflex that overrides the bradycardia to give tachycardia.
  - Graph: stimulus = arterial pO2. Signal = carotid body nerve discharges.
    - Normal resting pO2 = 100mmHg.
    - It's designed to pick up drops in O2 levels.
    - If pO2 goes up, there's no real change in nerve discharge. It really fires when pO2 drops.



Reflex outputs

- Input = from baroreceptors + chemoreceptors. Output = from PNS + SNS.
  - Note: blue means inhibitory, red means excitatory.
  - Why blue being applied to baroreceptors and red to chemoreceptors?
    - This is bc if the baroreceptors fire, they result in negative feedback + reduce in BP.
    - If chemoreceptors fire (bc of low pO2) they excite brain to cause increased respiration + vasoconstriction + tachycardia.



- **Efferent cardiovascular outputs**
  - **Sympathetic excitatory effect on:**
    - Heart
      - To increase contractility + HR.
    - Vessels
      - To cause vasoconstriction + increase TPR in arterioles.
      - To cause venoconstriction in veins – which will increase venous pressure and increase filling of the heart and transfer blood from venous to arterial side of circulation for benefit of BP.
    - Kidneys
      - To cause release of renin.
  - **Parasympathetic inhibitory effect on:**
    - Heart
      - To decrease HR.
- **Patterned efferent CV outputs**
  - Brain has a series of patterned outputs using PNS + SNS.
  - They are not simple pressor or depressor outputs (e.g. don't cause vasoconstriction to all organs).
  - The pattern targets specific vascular beds.
  - E.g. hypoxia causes:
    - Vasoconstriction in renal, muscle & gut arteries.
    - Vasodilation in heart arteries.
    - Neutral in cerebral arteries (as always).