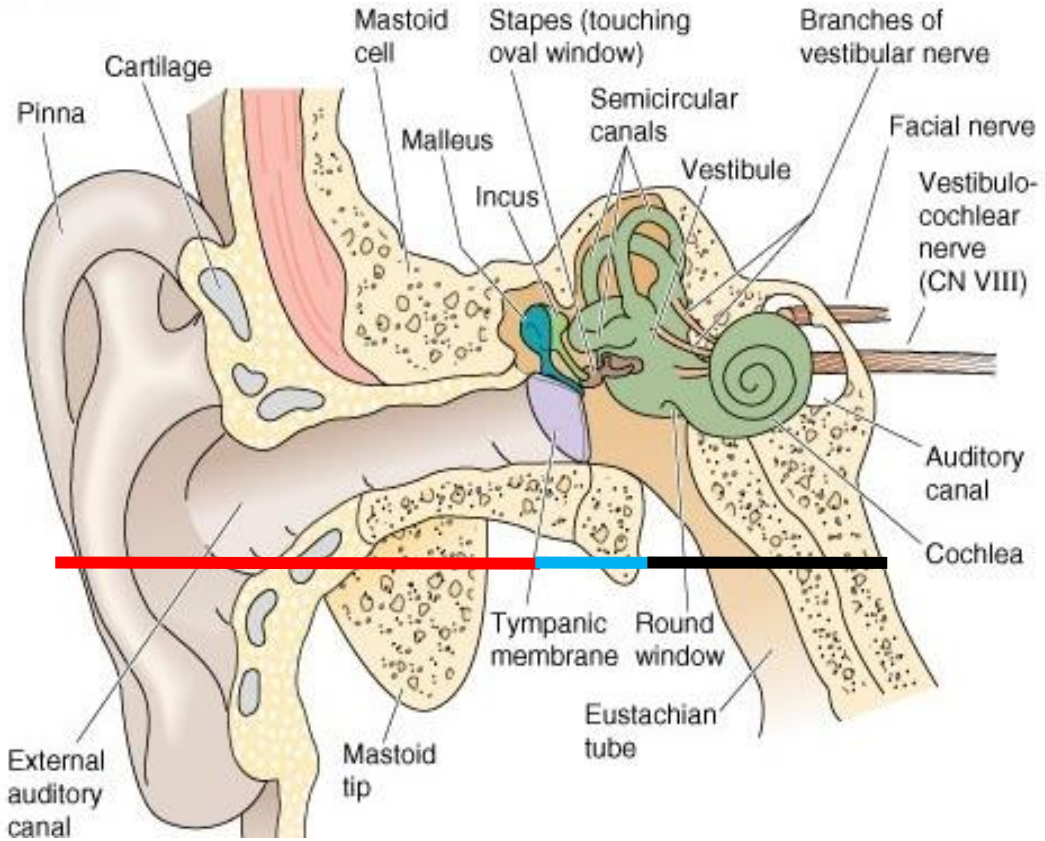
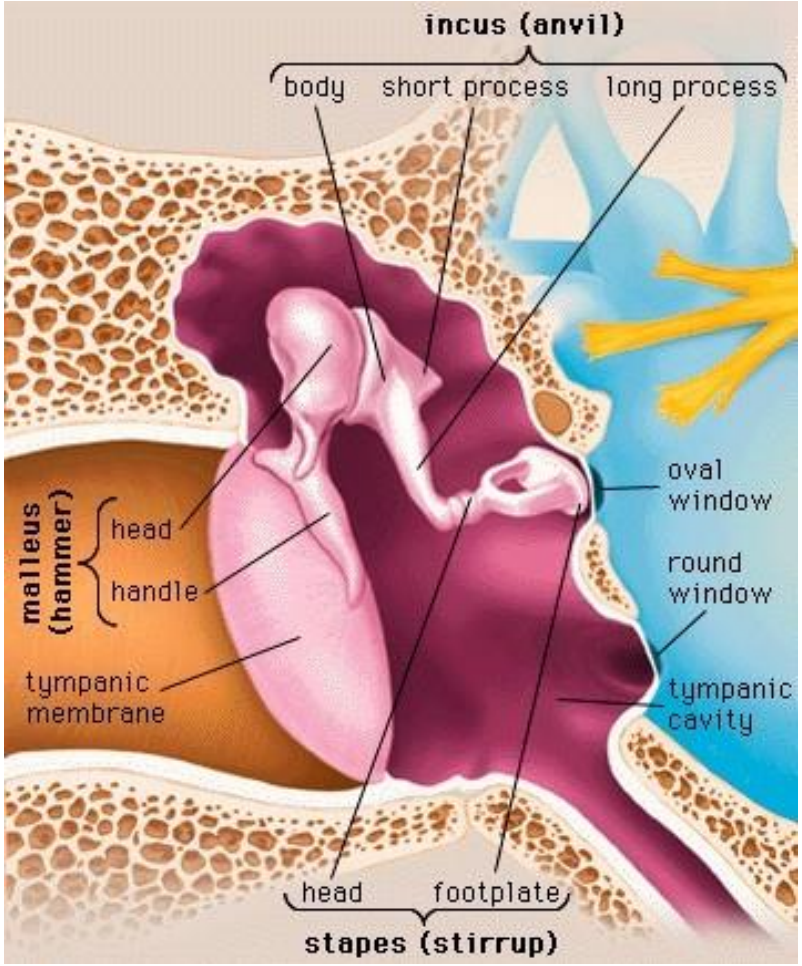
Auditory System

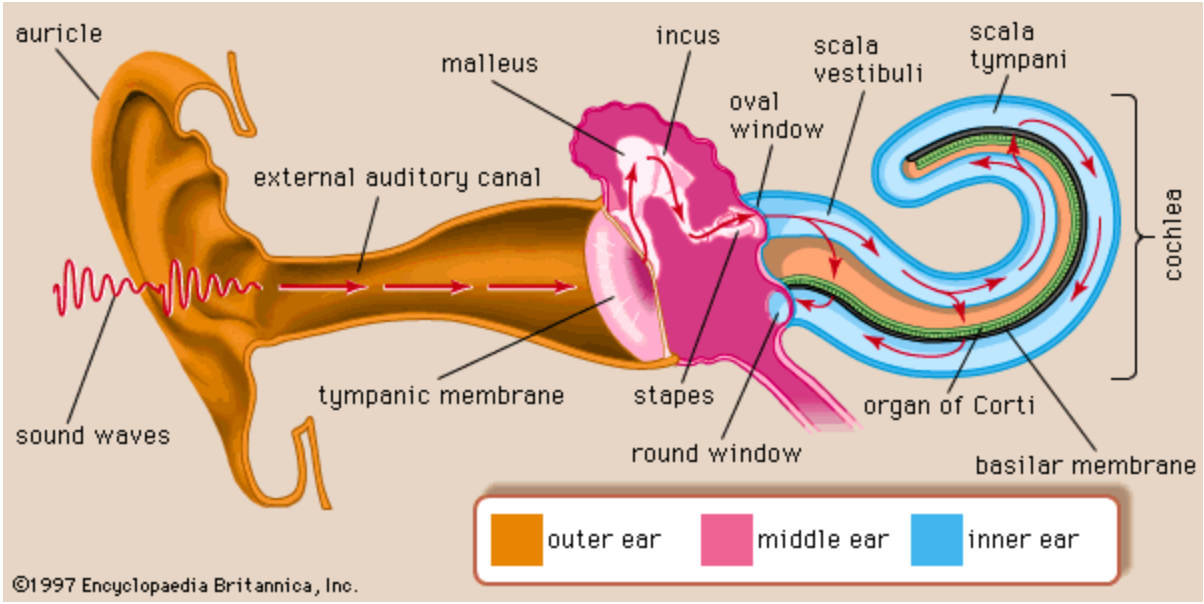
Dr. Goutam Dutta
Assistant Professor
Dept. of Physiology
Prabhat Kumar College, Contai

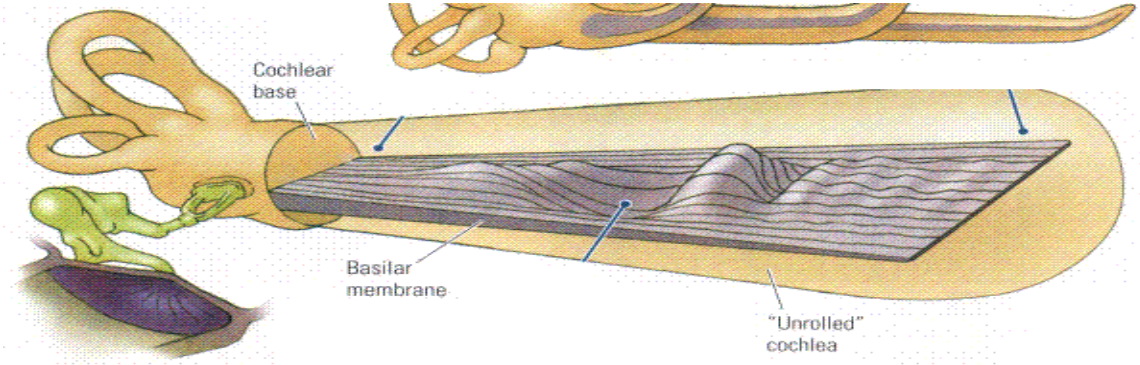

Mastoid cell
Stapes (touching oval window)
Branches of vestibular nerve
Cartilage
Pinna
Semicircular canals
Facial nerve
Malleus
Vestibule
Incus
Vestibulo-cochlear nerve (CN VIII)
Auditory canal
Cochlea
Tympanic membrane
Round window
Eustachian tube
External auditory canal
Mastoid tip

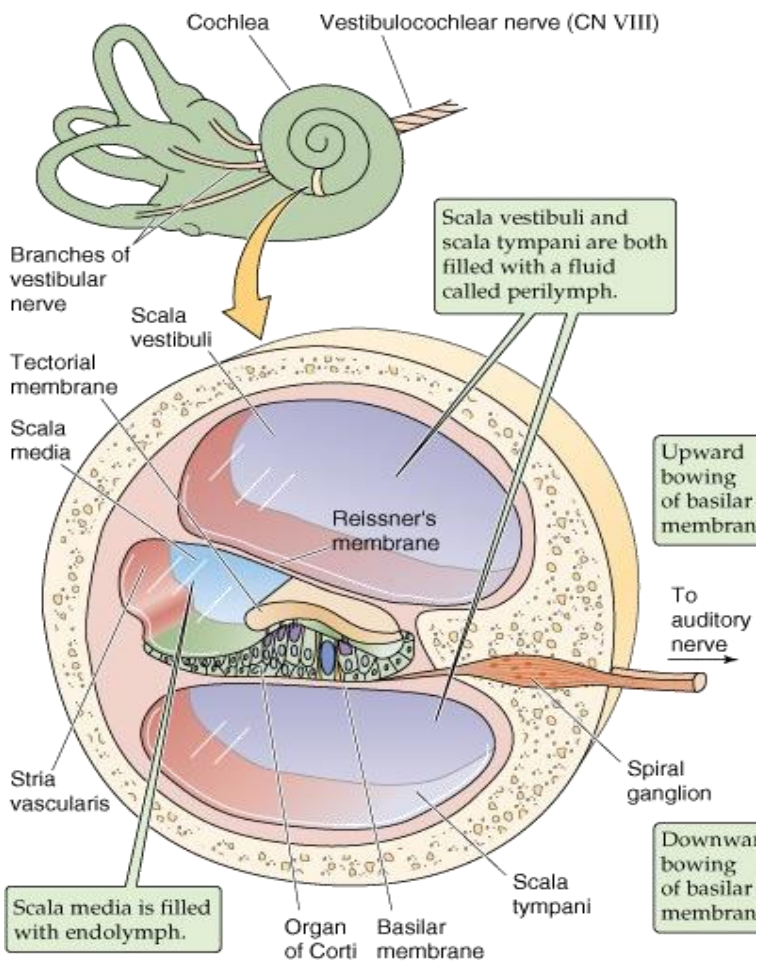
Introduction

- Snail-shaped osseous structure
- Coiled 2 & 2/3 turns around a central axis – Modiolus
- With in the bony cochlea (osseous labyrinth) lies the membranous labyrinth, consisting of –
  - Central scala media – cochlear duct
  - Superiorly, Scala vestibuli separated by Reissner's membrane
  - Inferiorly, Scala tympani separated by basilar membrane
- The connection of scala vestibuli with the middle

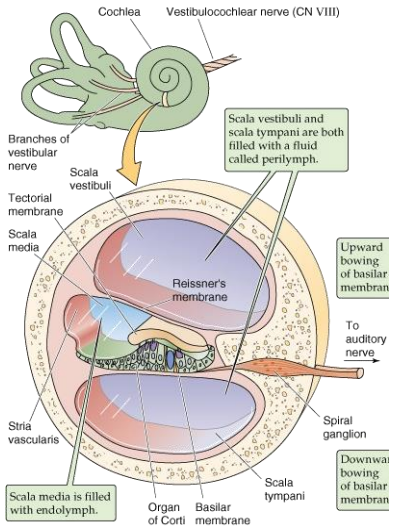

incus (anvil)
body
short process
long process
malleus (hammer)
head
handle
tympanic membrane
oval window
round window
tympanic cavity
head
footplate
stapes (stirrup)


auricle
malleus
incus
scala vestibuli
scala tympani
oval window
external auditory canal
cochlea
tympanic membrane
stapes
organ of Corti
sound waves
round window
basilar membrane
outer ear
middle ear
inner ear
©1997 Encyclopaedia Britannica, Inc.


Cochlear base
Basilar membrane
"Unrolled" cochlea

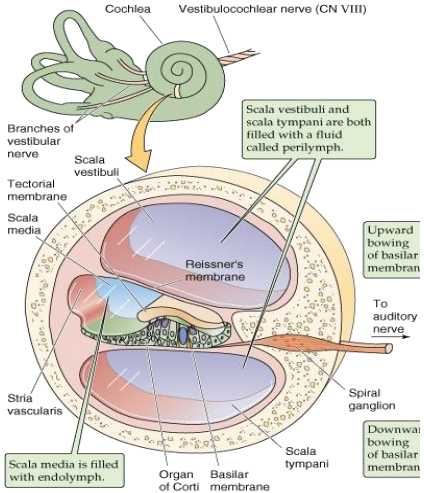

Cochlea
Vestibulocochlear nerve (CN VIII)
Branches of vestibular nerve
Scala vestibuli and scala tympani are both filled with a fluid called perilymph.
Scala vestibuli
Tectorial membrane
Scala media
Upward bowing of basilar membran
Reissner's membrane
To auditory nerve
Stria vascularis
Spiral ganglion
Downwa bowing of basilar membran
Scala tympani
Scala media is filled with endolymph.
Organ of Corti
Basilar membrane

- The Round window links the scala tympani to the middle ear & is covered by Round window membrane
- The scala vestibuli & scala tympani merge at the apex of cochlea – Helicotrema, & scala media ends blindly
- S.V. & S.T. are filled with perilymph, extracellular fluid with High Na+ & Low K+
- S.M. is filled with endolymph, composed of High K+ & Low Na+
- Cochlear Endolymph has electrical potential of +85mV
- This difference in ion composition and electrical potential difference provide energy for cochlea's

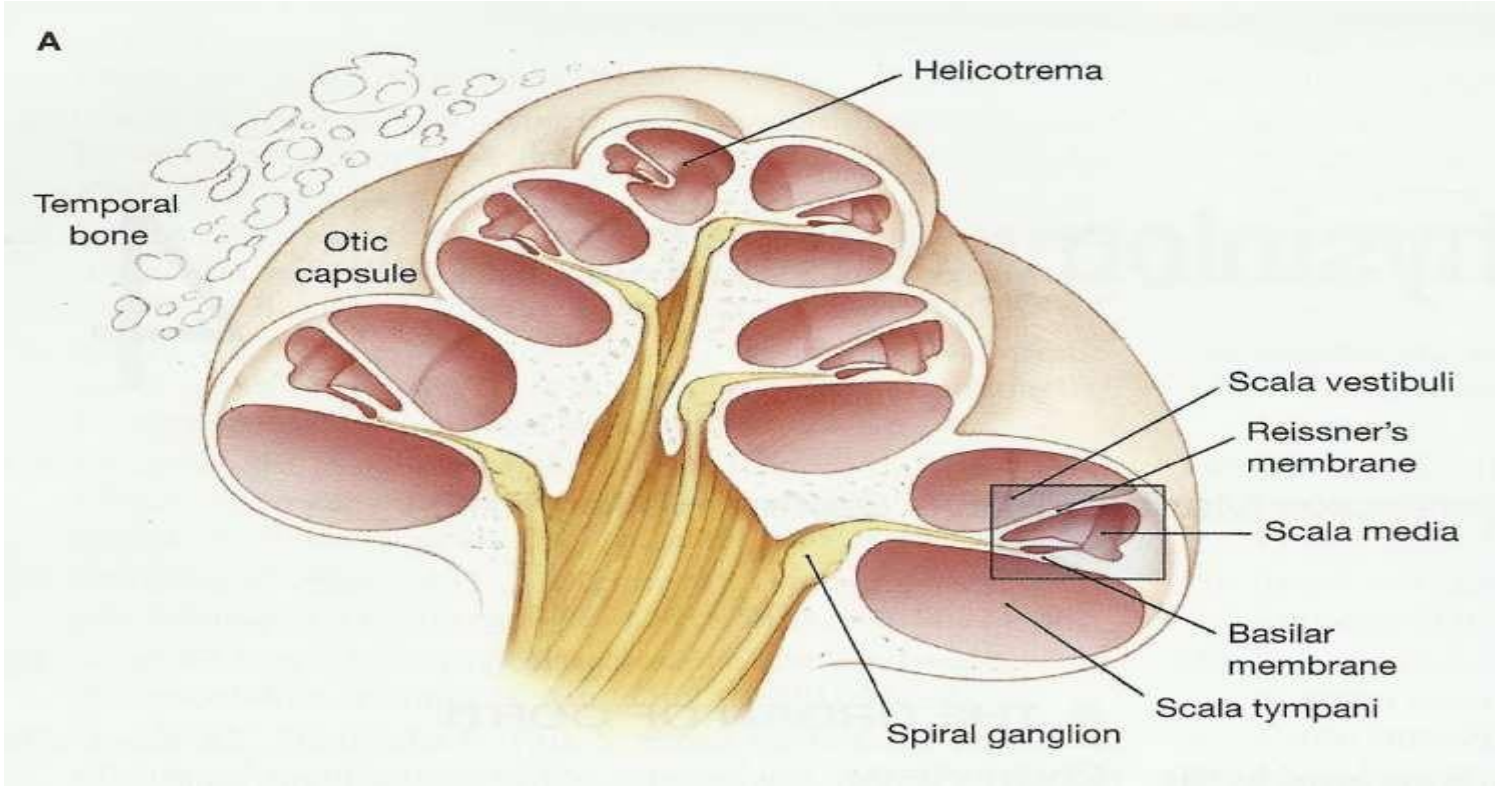


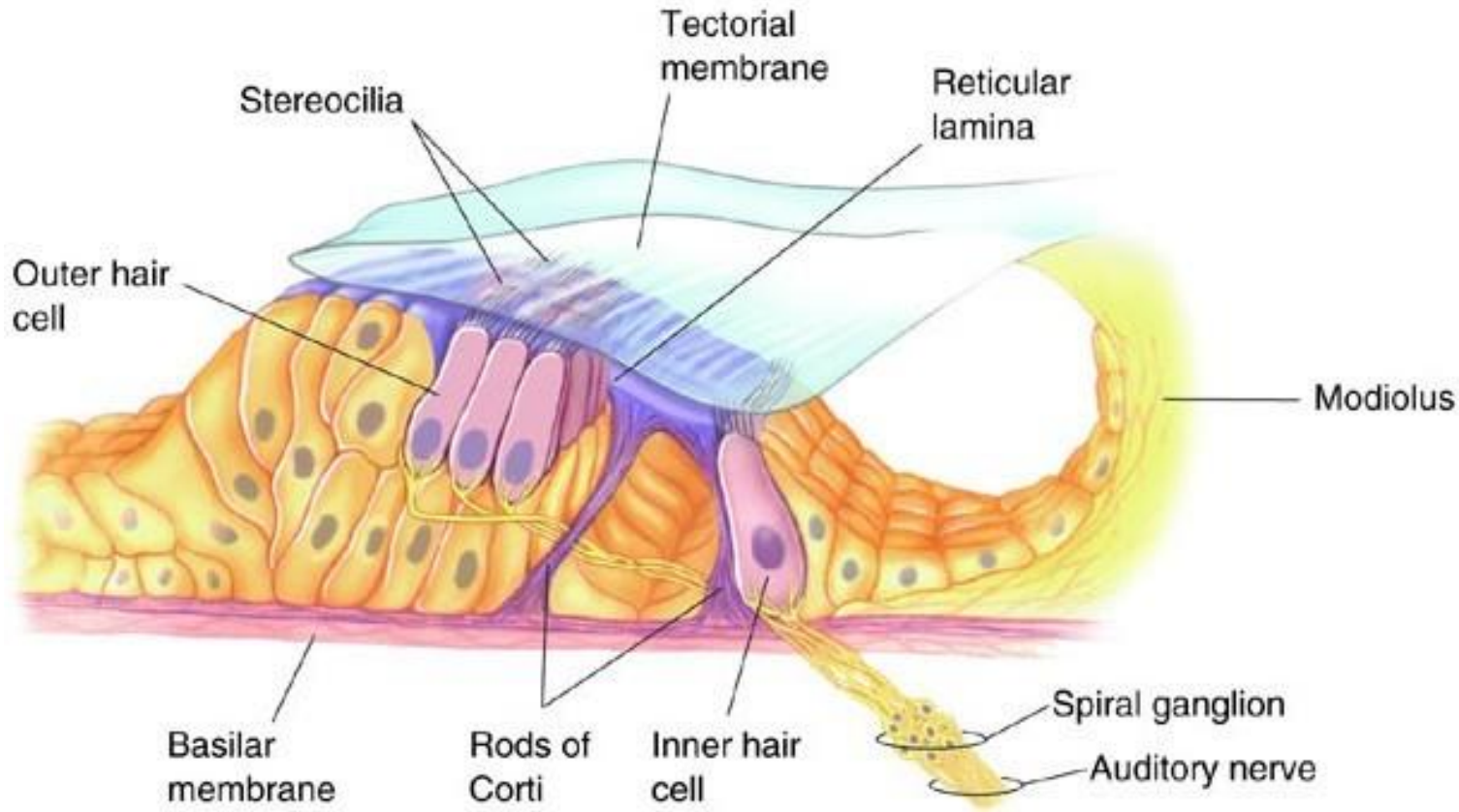
Ions	PERILYMPH	ENDOLYMPH
Na+	148	1.3
K+	4.2	157
Ca+	1.3	0.023
Cl-	119	132
HCO3-	21	31
pH	7.3	7.5

- Functional units of cochlea
  - The Organ of Corti – sensor of cochlea, converts & amplifies mechanical sound to electrical signals (Mechano-electrical Transduction)
  - Stria Vascularis – cochlea's battery, generates energy (Endocochlear potential)
  - The Spiral Ganglion – these are neurons featuring axons, electrical wires, transporting signals from cochlea to CNS.



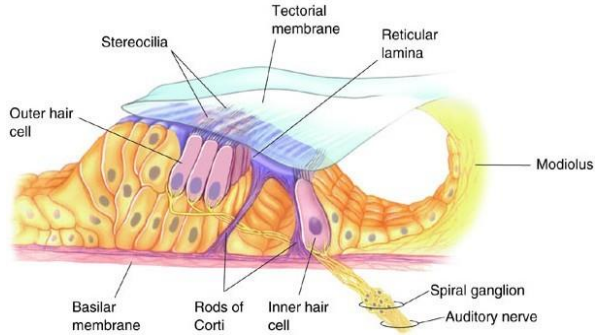
Cross-section of Cochlea



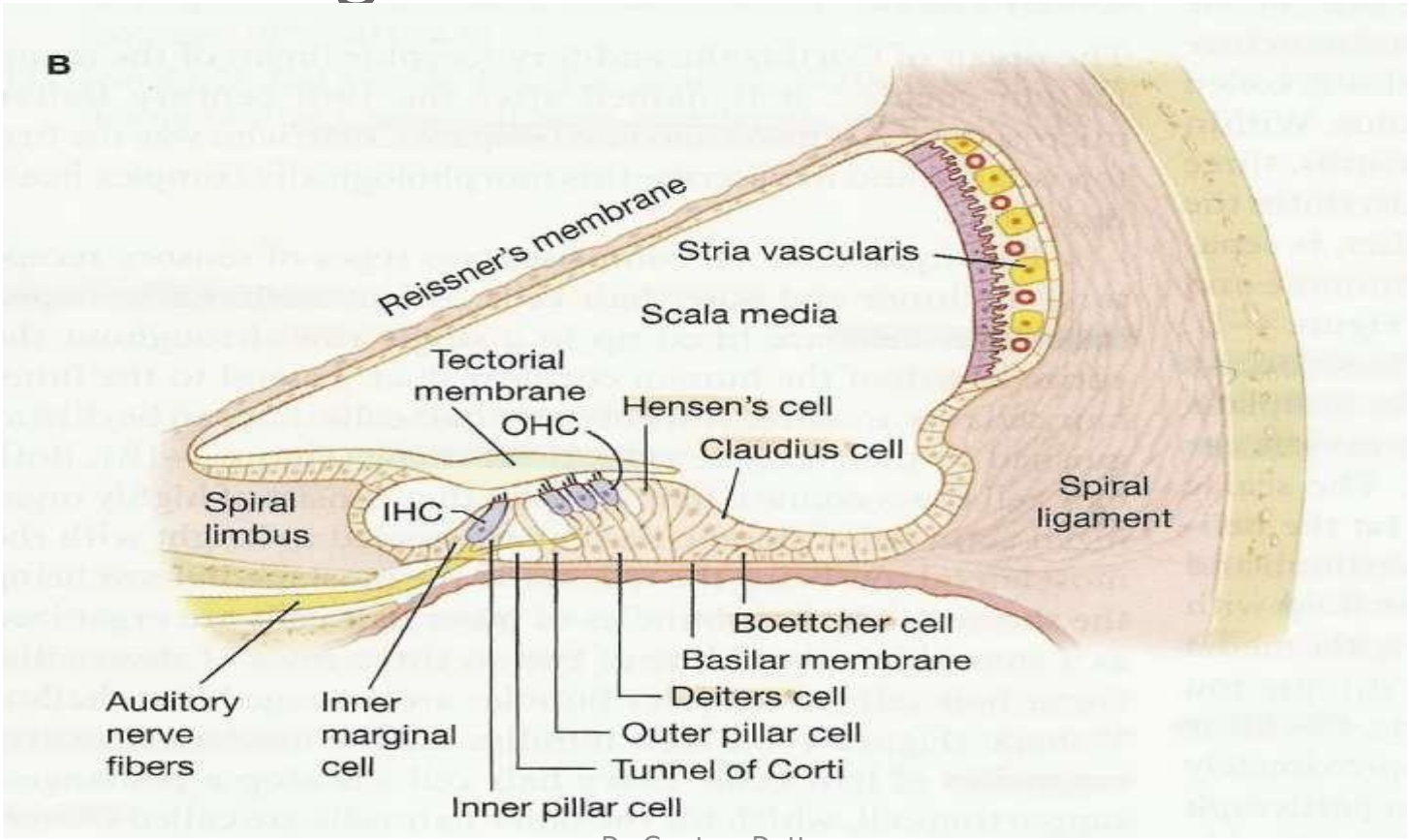

Tectorial membrane
Stereocilia
Reticular lamina
Outer hair cell
Modiolus
Spiral ganglion
Auditory nerve
Basilar membrane
Rods of Corti
Inner hair cell

THE ORGAN OF CORTI

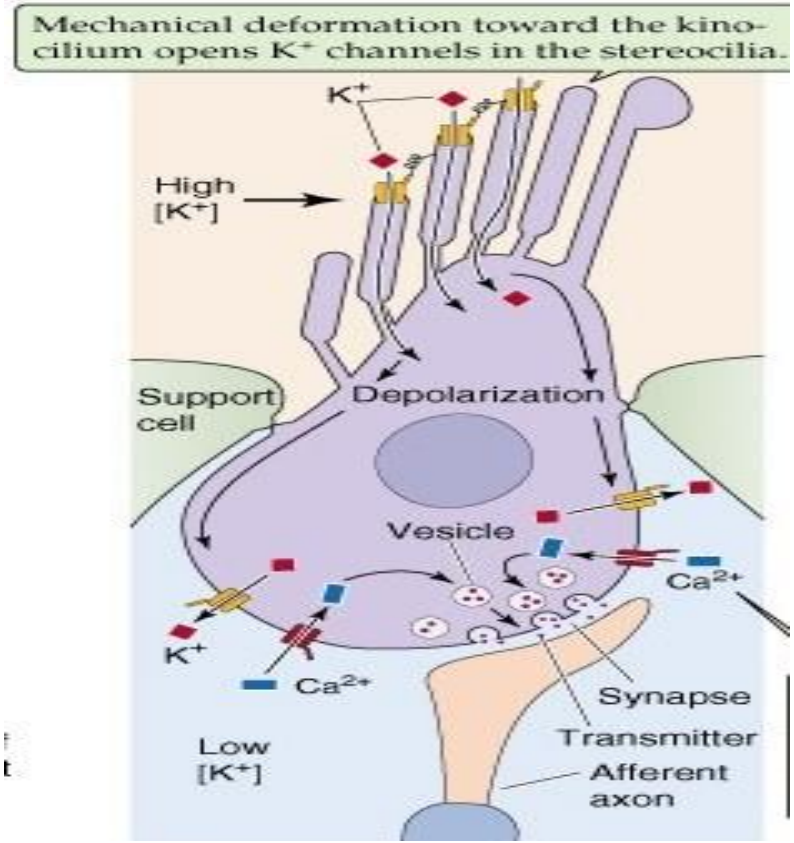
- Named after – Alfonso Giacomo Gaspare Corti
- It consists of two types of sensory receptors – inner and outer hair cells
- There are about 3500 flask shaped Inner Hair Cells, lined up in a single row, through out entire length of S.M.
- Lateral to IHC's lies 3 rows of Outer Hair Cells, cylindrical shaped.
- They contain hair bundles consists of Actin-filled stereocilia, graded acc. to height, with the most lateral being the tallest and most medial row being the shortest.



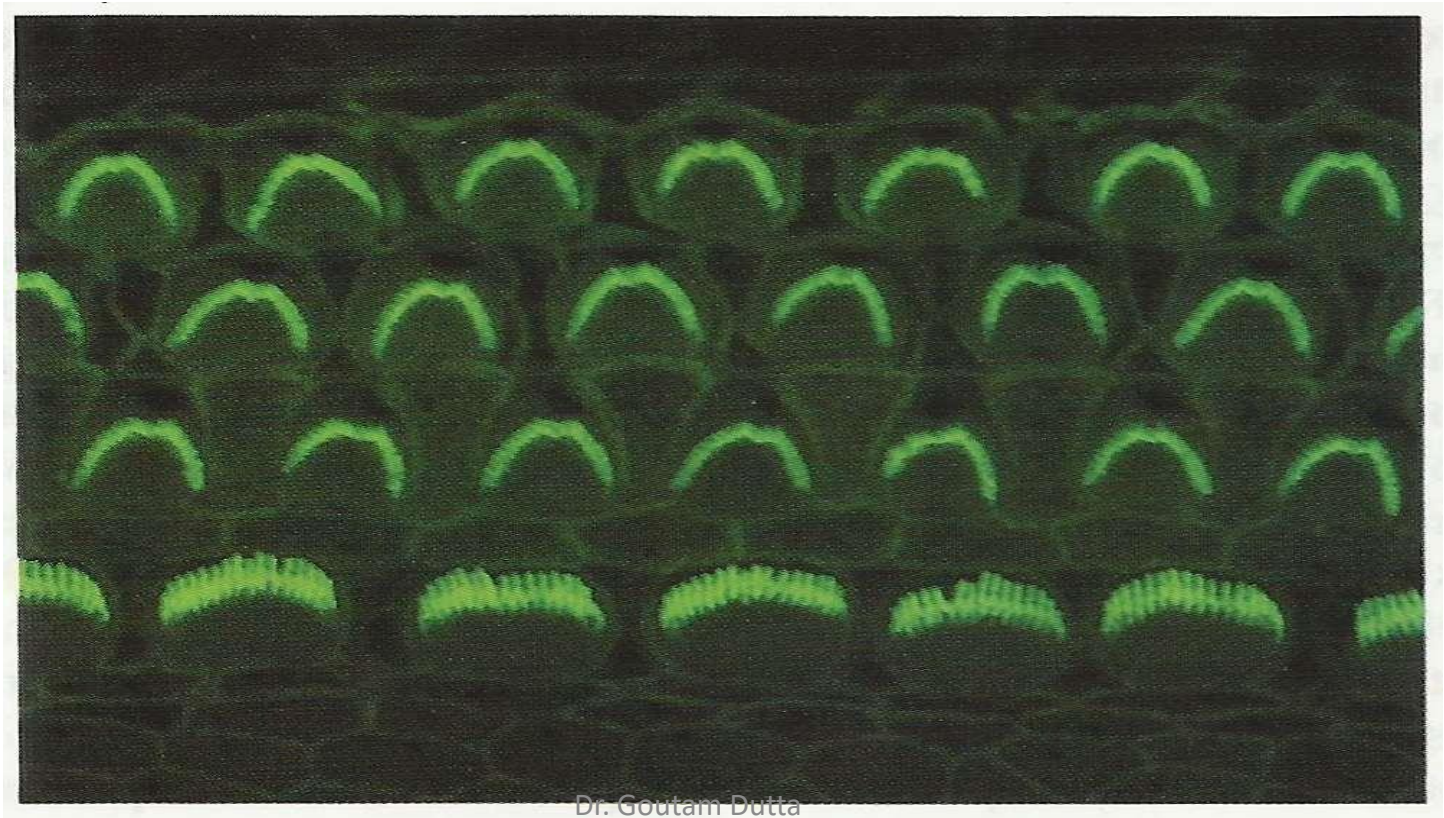
The Organ of Corti & surr. structures

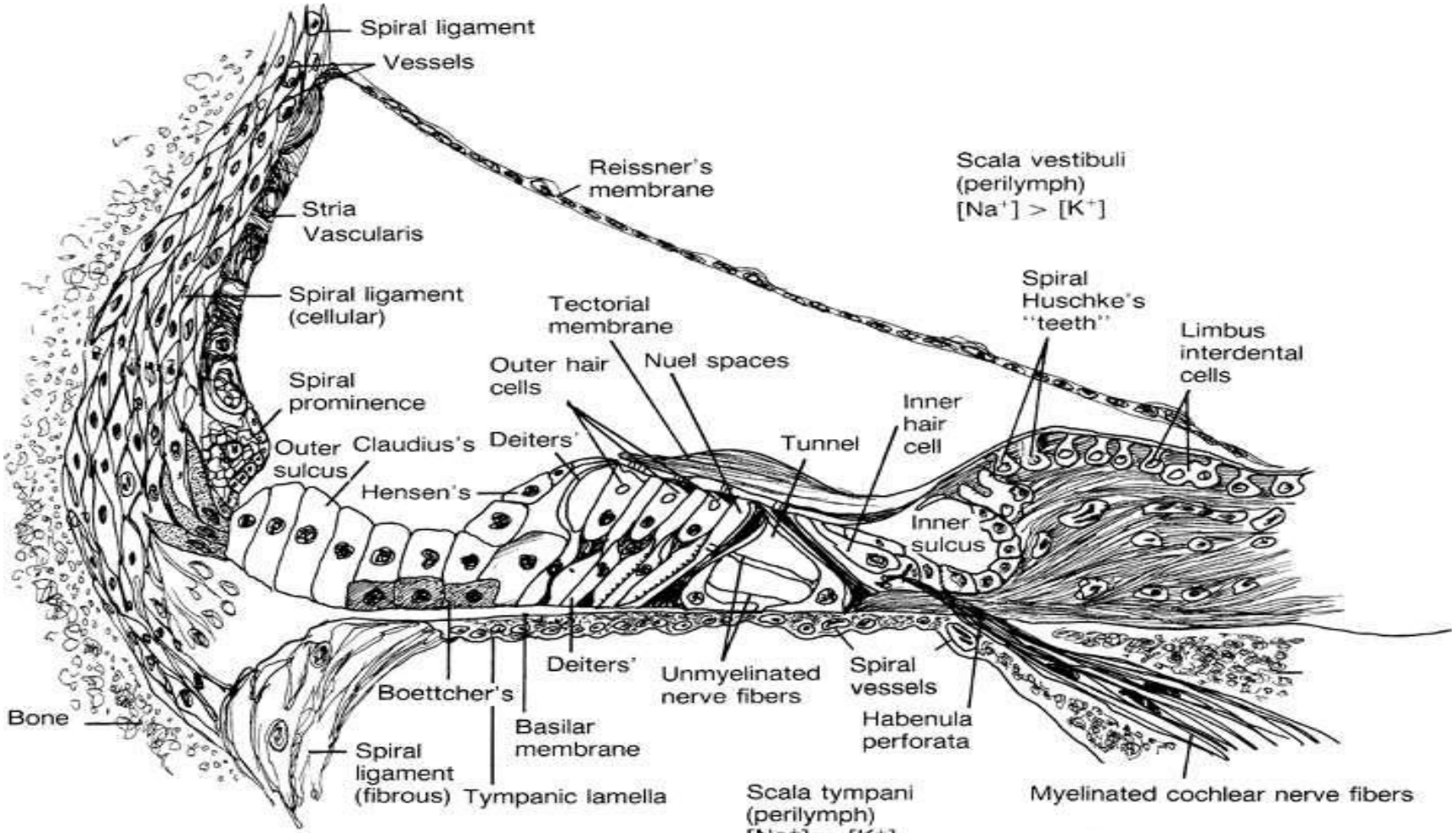


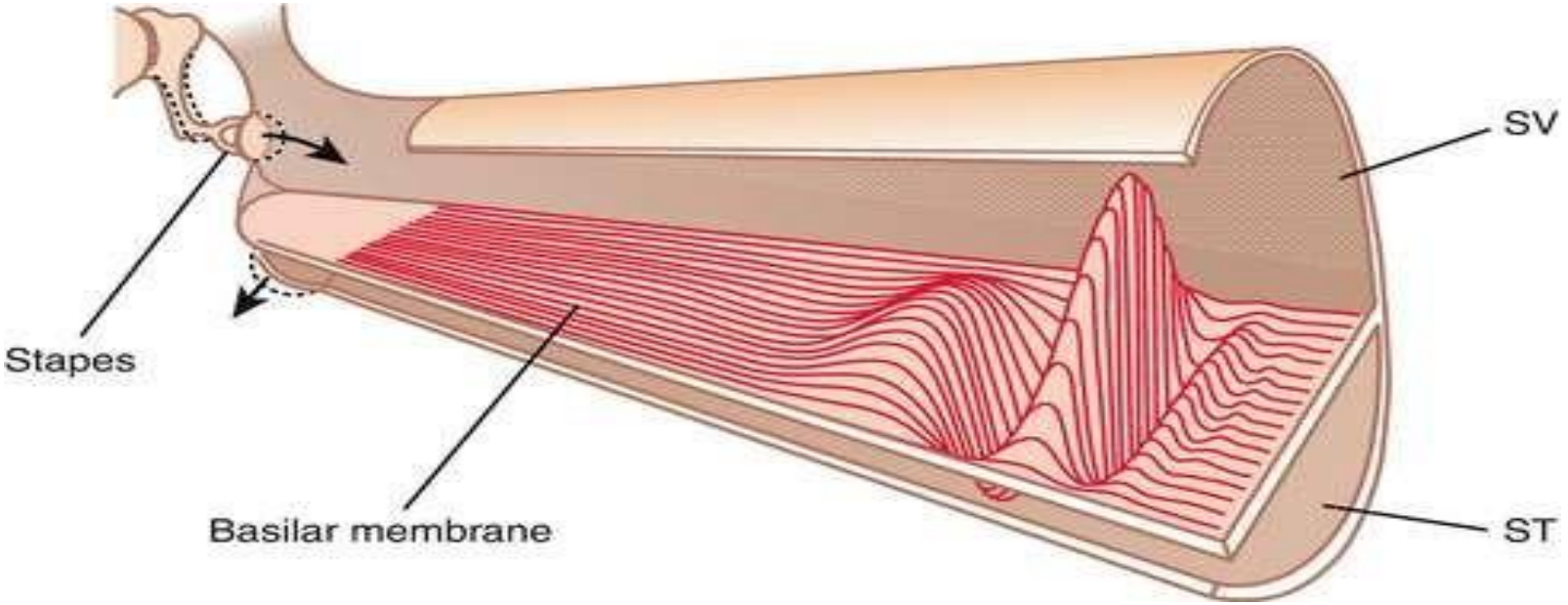
- The hair bundles of IHC's are organized as a smooth curved line of 2-3 rows of stereocilia & OHC's stereocilia bundles are arranged in a shallow V-shape.
- They are Mechano-sensitive organelles of H.C.'s
- Every H.C. sits over a phalangeal supporting cell, i.e. Deiters Cells for OHC's
- The inner and outer pillar cells delienate the area between
- IHC's & OHC's framing the Tunnel of Corti
- Other supporting cells embrace the hair cell-bearing part of organ of corti

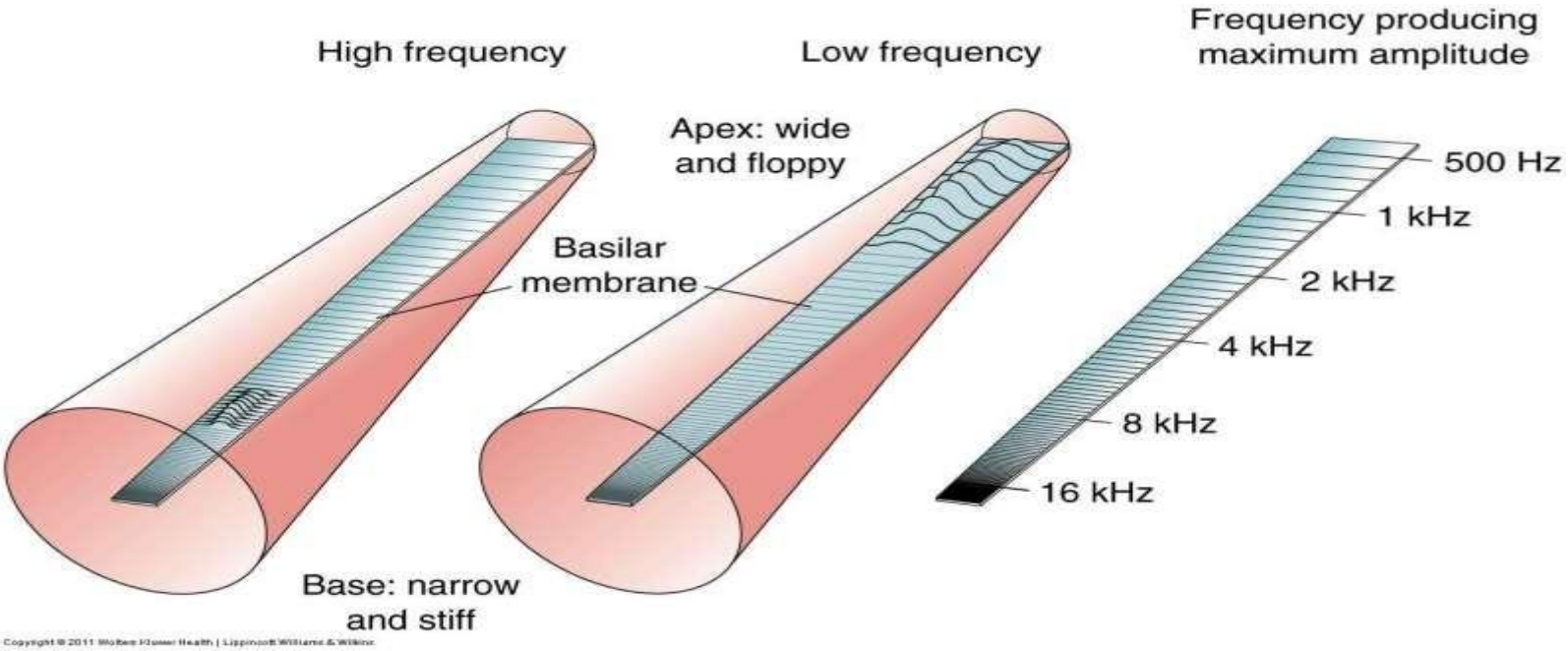


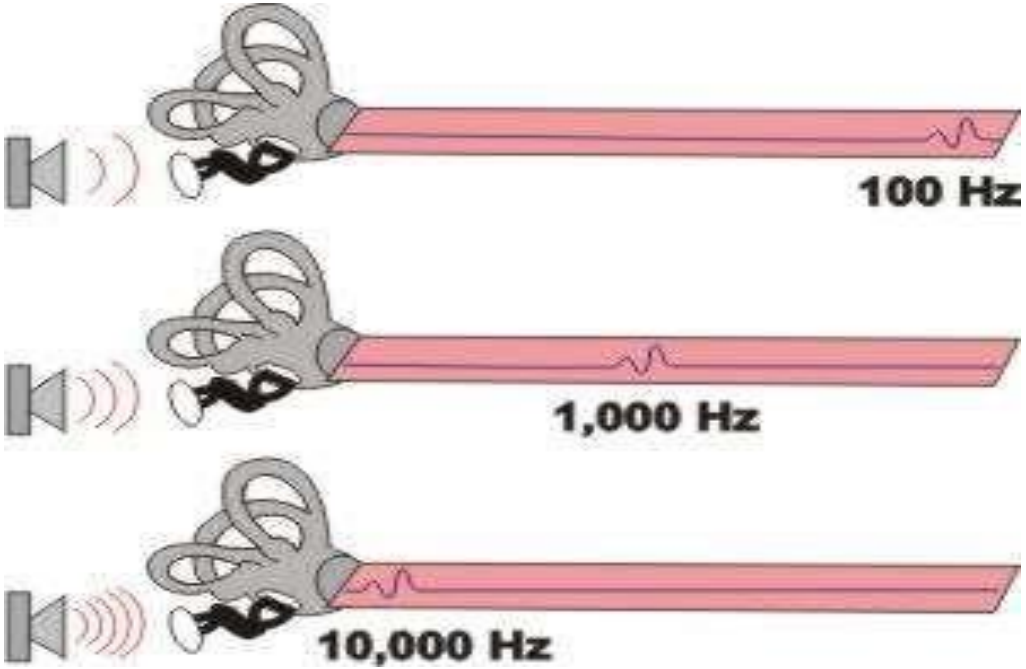
Cochlear Stereocilia




Spiral ligament
Vessels
Reissner's membrane
Scala vestibuli (perilymph) [Na+] > [K+]
Stria Vascularis
Spiral ligament (cellular)
Tectorial membrane
Spiral Huschke's "teeth"
Limbus interdental cells
Outer hair cells
Nuel spaces
Spiral prominence
Inner hair cell
Outer sulcus
Claudius's
Deiters'
Tunnel
Hensen's
Inner sulcus
Deiters'
Unmyelinated nerve fibers
Spiral vessels
Boettcher's
Bone
Basilar membrane
Habenula perforata
Spiral ligament (fibrous)
Tympanic lamella
Scala tympani (perilymph) [Na+] > [K+]
Myelinated cochlear nerve fibers

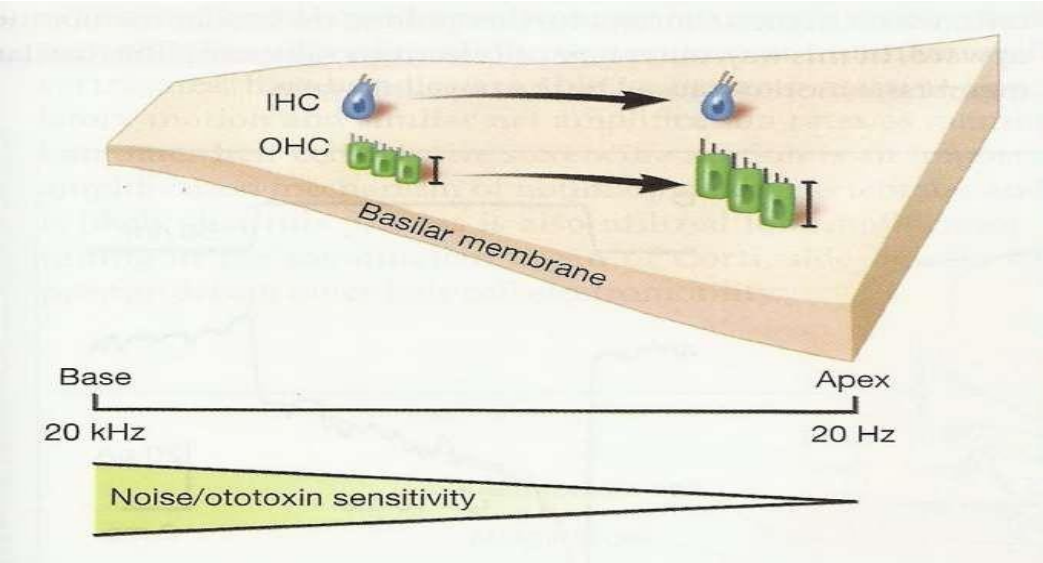

SV
Stapes
Basilar membrane
ST


High frequency
Low frequency
Frequency producing maximum amplitude
Apex: wide and floppy
Basilar membrane
Base: narrow and stiff
500 Hz
1 kHz
2 kHz
4 kHz
8 kHz
16 kHz


100 Hz
1,000 Hz
10,000 Hz

- A pure tone stimulus, the travelling wave moves from base to apex, reaches a Maximum* at a characteristic place along basilar memb. and then decays
- This precise location of this Maximum depends on Frequency of stimulus – the principle of tonotopic organisation of cochlea
- The base is tuned for frequencies of 20 kHz and apex for 20 Hz
- The tonotopic gradient is a continuous gradient in basilar membrane width and also with changes in hair cell height and length of cellular structures i.e. stereocilliary hair bundles

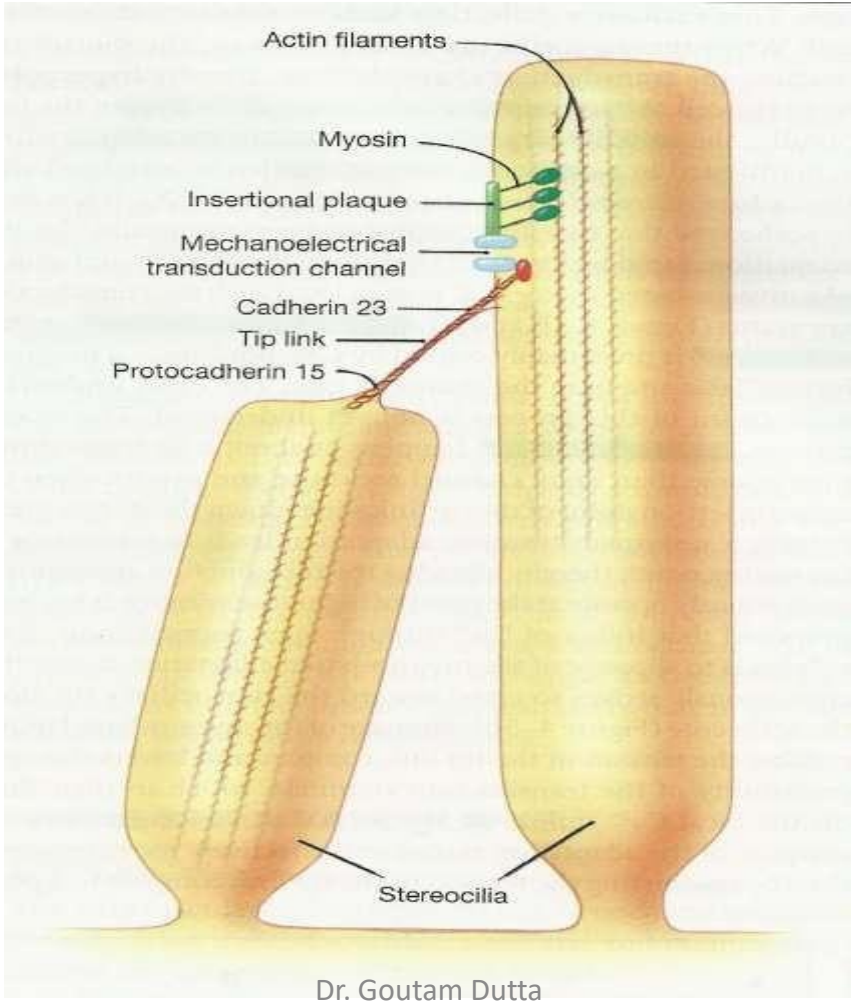
Tonotopic organization of Organ of Corti



Inner Hair Cells & Mechanoelectrical Transduction

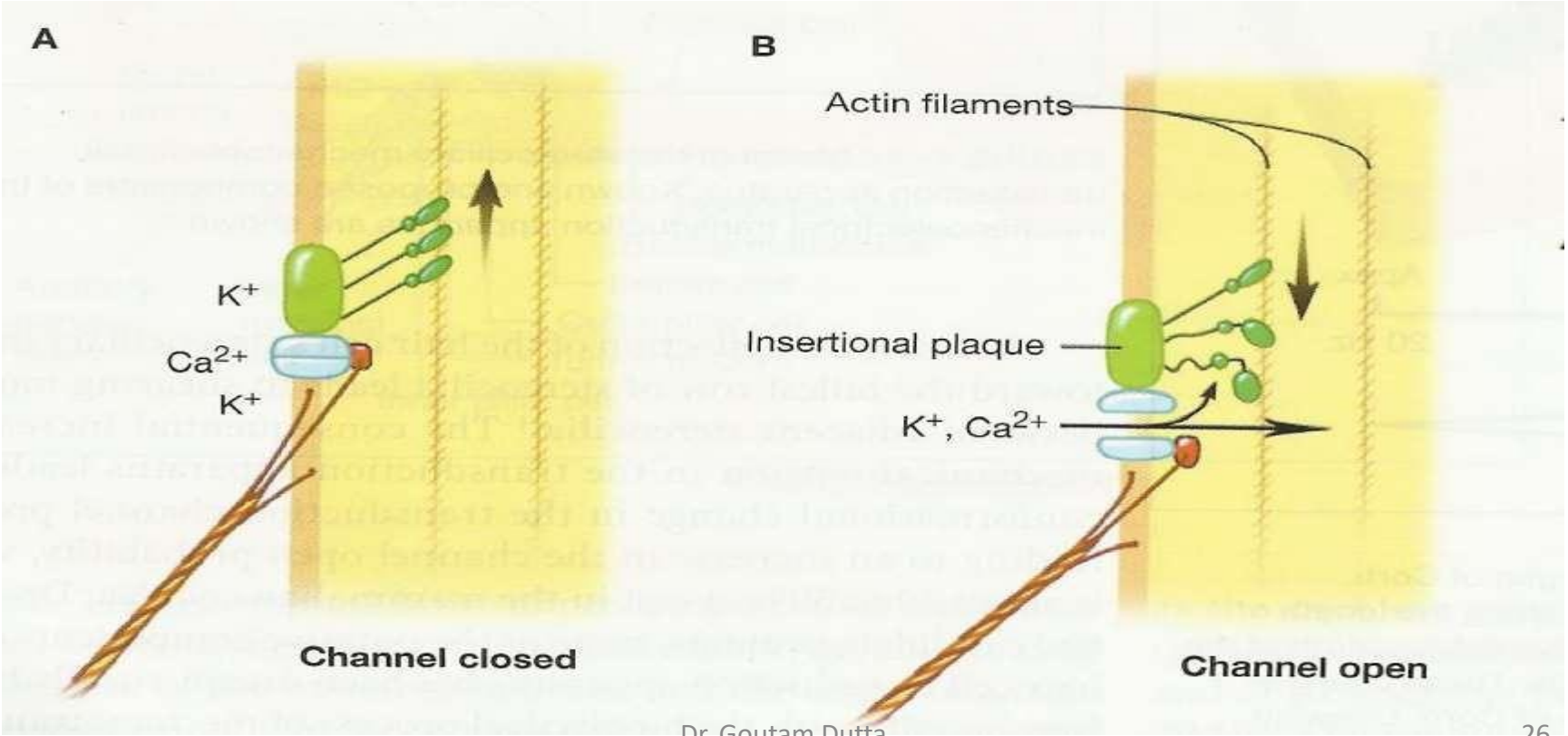
- The IHC's are sensory cells which convert mechanical stimulation to electrical signals and the synaptic activity is transmitted to brain
- This M-E Transduction occurs at tips of stereocilia
- This apparatus is present in all hiar cells & consists of mechanically gated ion channels, that is closely asso. with elastic structures & a Tip-link, that connects the tip of the stereocilium to the side of the next tallest stereocillium

- Components of Stereocilia
  - Cadherin 23 & Protocadherin 15 – components of Tip-Link
  - Mechano-Electrical Transduction channel
  - Insertional Plaque
  - Myosin 1C
  - Actin filaments
- Mechanical deflection of hair cell bundles leads to mechanical tension leading to conformational change in transduction channel protein & increase in channel opening
- USHER SYNDROME - Congenital Hearing Loss
  + Progressive loss of vision due to Retinitis Pigmentosa


Actin filaments
Myosin
Insertional plaque
Mechanoelectrical transduction channel
Cadherin 23
Tip link
Protocadherin 15
Stereocilia

- On mechanical stimulation
  - Towards the TALLEST row of stereocillia – K+ & Ca++ ions enter hair cell through open M-E T channels, located near the tips – leads to DEPOLARISATION of cell
  - Towards the SHORTEST stereocillia, the M-E T channels close – leads to HYPERPOLARISAITON of cell
- After a sustained excitatory deflection of hair bundle, the initial large transduction current ADAPTS, manifesting as decline of current – correlated with closure of transduction channels
- 2 distinct process involved in adaptation
  1. Rapid reclosure of transduction channels
  2. Sliding of myosin based motor asso. with

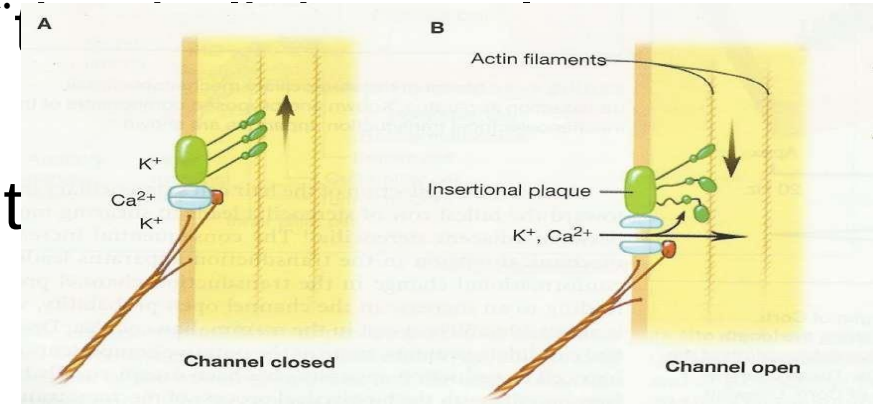
Mechanoelectrical Transduction



- 1st - Rapid Channel reclosure "FastAdaptation"
  - Ca++ binding to intracellular site near ch. gate
- 2nd - "SlowAdaptation"
  - 10 tmies slower than Fast Adap.
  - Upper tip-link slides down the stereocilum

- During sustained stimulus, adaptation leads to resetting of restore point, hence allowing the transduction apparatus to function at point of highest sensitivity
- The influx of Ca++ through open transduction channels leads to slippage of myosin based adaptation motor, which continuously strives to crawl towards the stereocilliary tip along actin core

- The slippage of the myosin based motor channels reduces the tension in the tip-link complex & lowers the open probability of the transduction channels, shutting off the Ca++ influx
- At Low Ca++ levels □ myosins of the adaptation motor will effectively move upwards □ readjusting the tension in a point where the open probabili the M-E T ch. is close to t open probability at rest.
- Myosin 1C is crucial for th adaptation t process



OUTER HAIR CELLS & AMPLIFICATION

- OHC's have a key role in amplification of Basilar memb. motion
- Amplification is necessary for detection of sounds at low pressure levels
- OHC's are mainly responsible for AMPLIFICATION & SHARP TUNING ofAuditory system
- Mechanism of Amplification –

  Somatic Electromotility the OHC's change their length by 3-5% in response to electrical stimulation

- When Depolarized, they Contract & when Hyperpolarized they Elongate
- The OHC's exert mechanical force causing movements of basilar memb. motion caused by the travelling wave
- Prestin – motor protein responsible for somatic electromotility in outer hair cells. It belongs to SLC26 anion transporter superfamily – mediate electroneutral exchange of chloride & carbonate across plasma membrane
- Hypothesis* - intracellular anions act as voltage sensors which bind to prestin and trigger confirmational changes
  - Hyperpolarisation □ anion binding to prestin □ increase in surface area of prestin □ cell elongation
  - Depolarisation □ dissociation of anion □ decrease in the prestin surf area □ cell contraction
  - At rest □ anions are usually bound to prestin □ longer

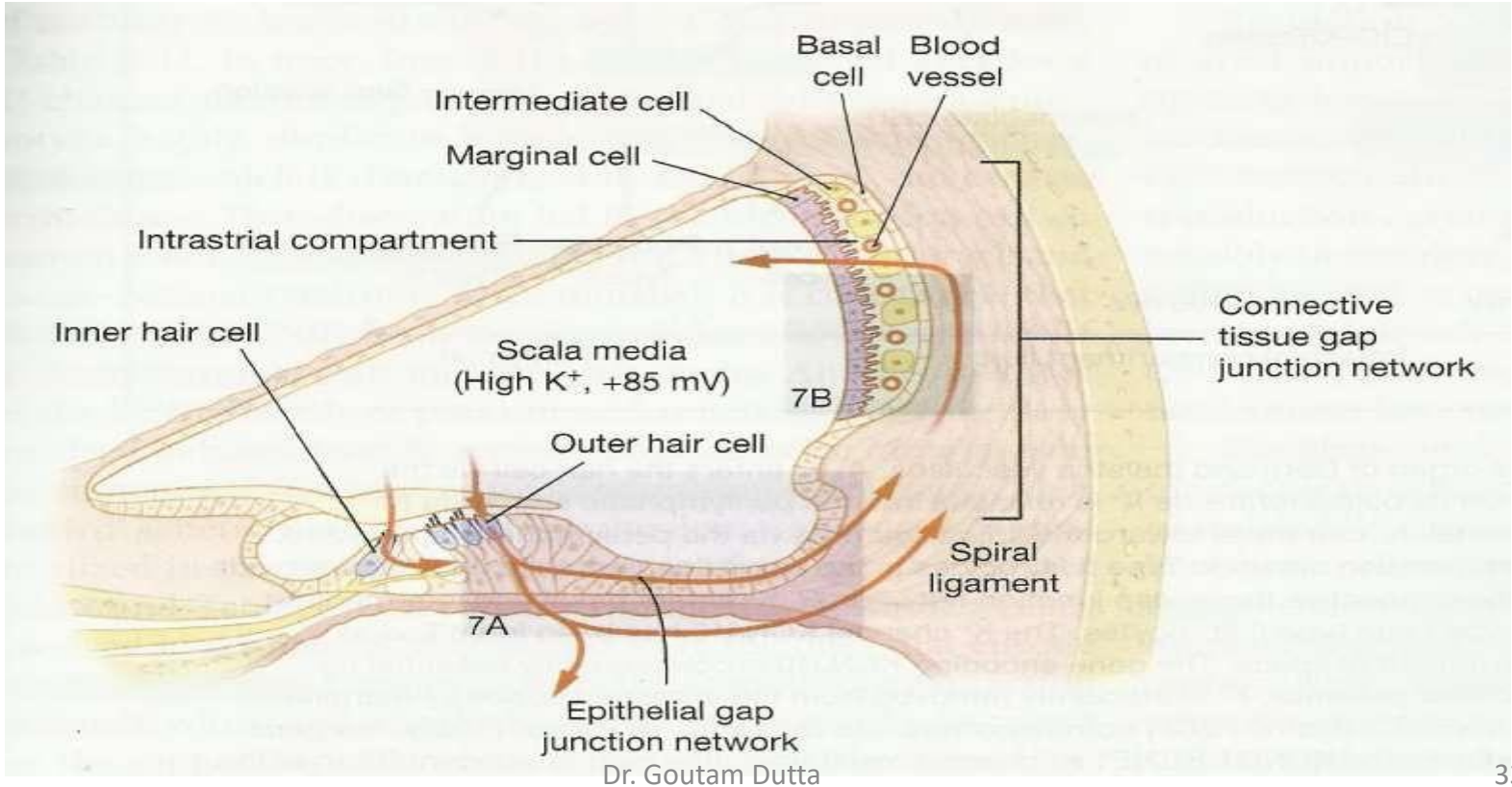
TECTORIAL MEMBRANE

- It is an extracellular structure overlying IHC's & OHC's & it changes its size from base to apex
- Only the tallest stereocillia of OHC's are directly embeded into the undersurface of tectorial membrane
- TM is attached on its inner edge to spiral limbus & is loosely connected to the supporting cells – Hensen's cells by trabeculae
- *Mutations in TM genes – Alpha & Beta Tectorin – caused profound hearing loss
- It is more like a resonant gel which is involved in enhancing the frequency selectivity of cochlea

STRIA VASCULARIS

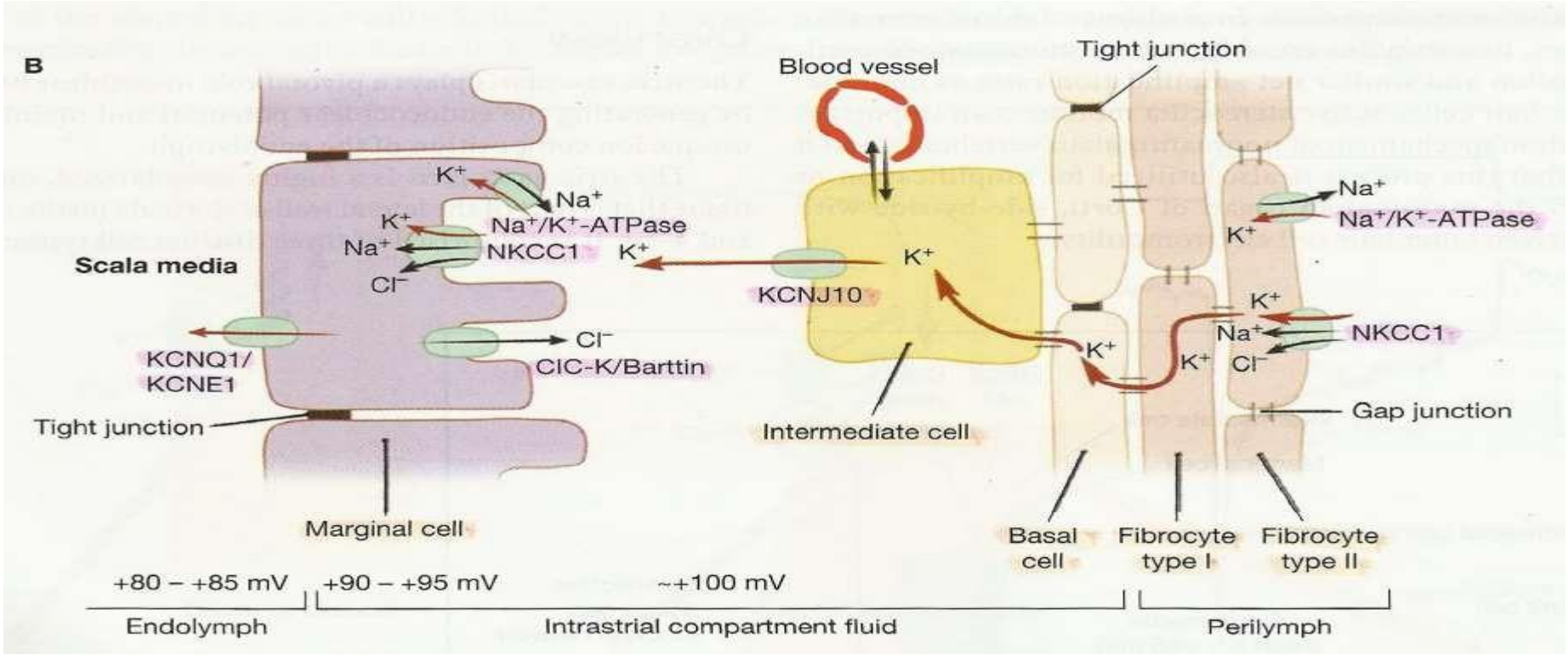
- Plays an important role in cochlear hemostasis by generating endocochlear potential & maintaining the unique ion compostion of endolymph
- Highly vascularized, multi-layered tissue & is a part of lateral wall of SM
- 3 distinct cell types
  - Marginal
  - Intermediate
  - Basal

Stria Vascularis & K+ Circulation



- Tight junction demarcate strial tissue & provide ionic barriers with marginal cells at one end & basal cells at other end
- The extracellular space between these two barriers is known as intrastrial compartment
- Marginal cells separate endolymph filled scala media from interstitial compartment that is filled with interstitial fluid
- Basal cells separate interstitial cells from perilymph that surrounds fibrocytes of the spiral ligament
- The intermediate cells as well as blood vessels are embeded in intrastrial compartment

Passage of ions from Perilymph to Endolymph in SV



- Gap junctions connect basal cells with with intermediate cells & with fibrocytes of spiral ligament – allowing Electric coupling & exchange of ions and small molecules
- The regulation of cochlear fluid homeostasis also involves endolymphatic sac, which responds to endolymph volume disturbance
- Malfunctions in cochlear fluid homeostasis due to disruptions of endocochlear potential, ionic composition, or its volume regulating mechanism leads to varios forms of hearing impariment

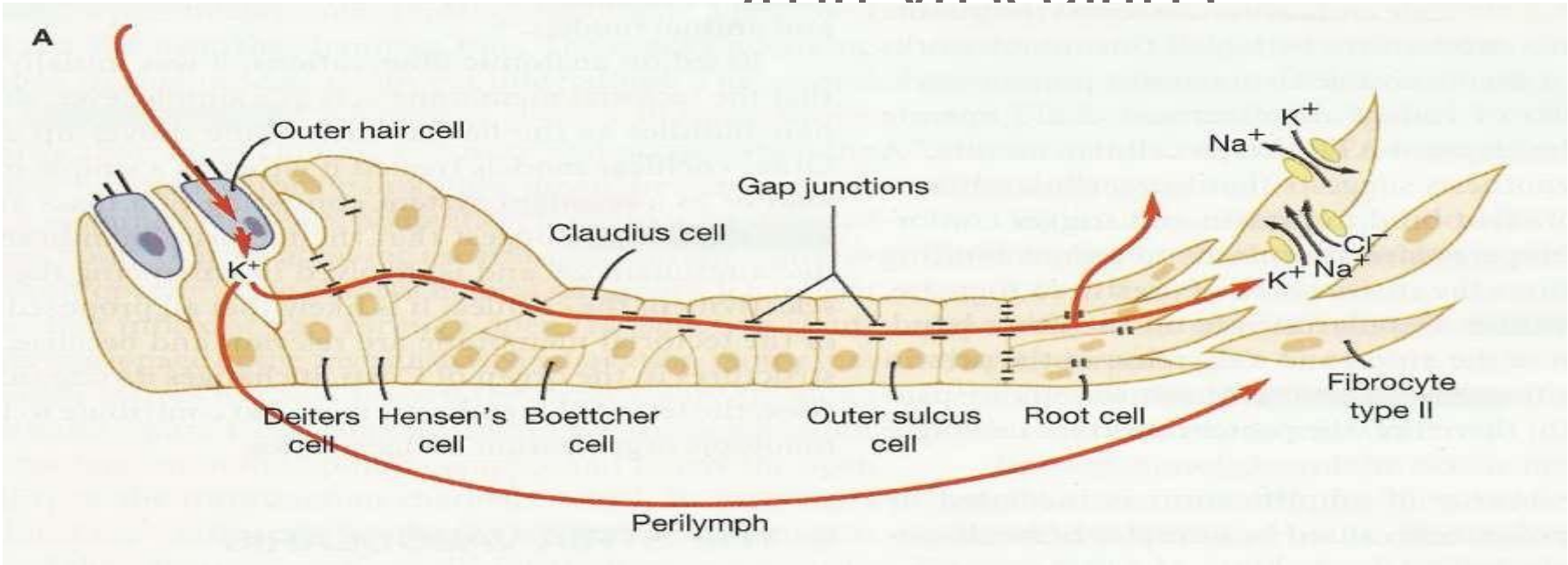
ENDOCOCHLEAR POTENTIAL & POTASSIUM HOMEOSTASIS

- Hair cell mechanoelectrical transduction works efficiently due to large driving force for cations to enter cell's cytoplasm from scala media
- The +85 mV endocochlear potential of endolymph & chemical gradient of K+ are the main components of the driving force

- HEARING THRESHOLD INCREASES APPROXIMATELY BY 1dB PER 1mV LOSS OF ENDOCOCHLEAR POTENTIAL

- K+ is the main cation of endolymph which generates endocochlear potential
- Movement of K+ in cochlea –
  1. K+ can enter hair cells through mechanoelectrical transduction channels & is released through hair cells' basolateral membranes into perilymphatic extracellular space
  2. K+ can enter supporting cells and move towards the spiral ligament by extensive gap junction network
  3. Alternatively, K+ can diffuse extracellularly via perilymphatic space
- Spiral ligament composed of Type II & Type I fibrocytes take up K+ and provide an intracellular pathway into basal & intermediate cells of stria vascularis

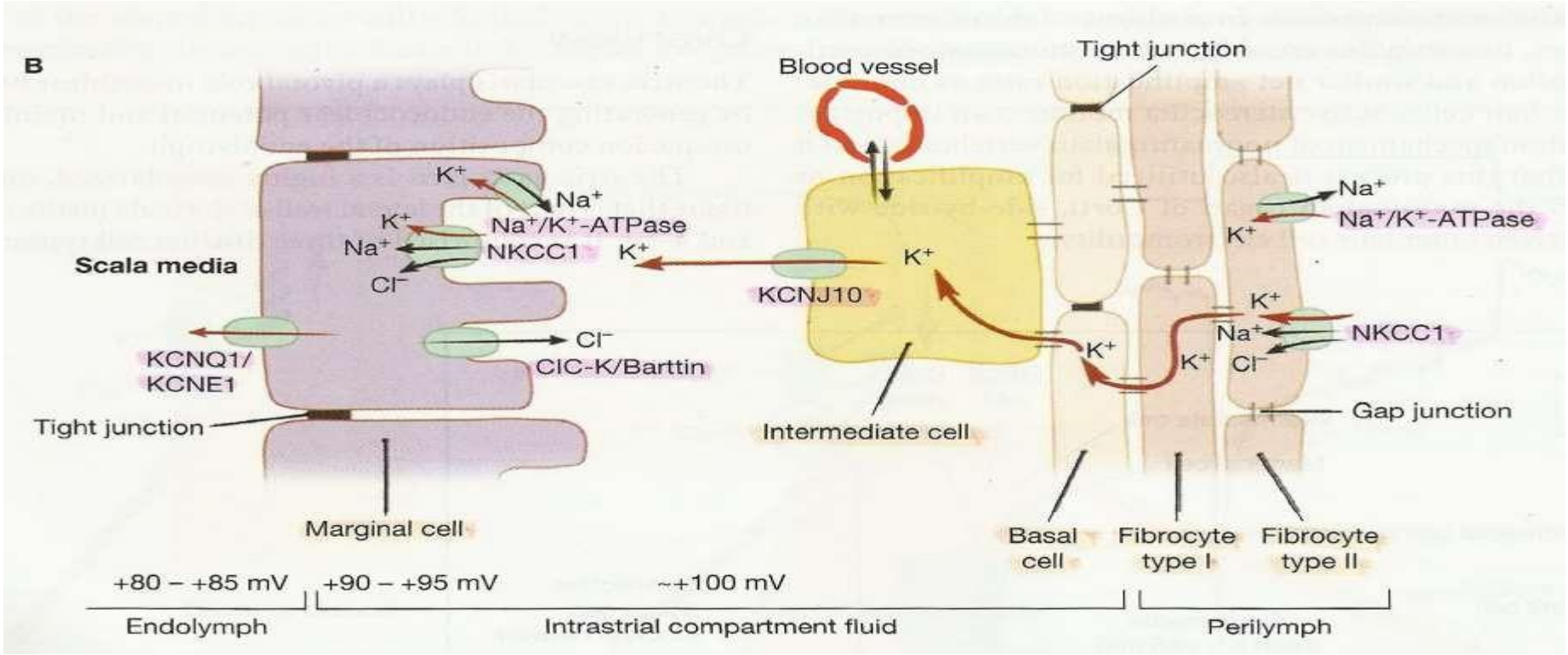
K+ flow through the Organ of Corti & Stria Vascularis



- K+ is released by intermediate cells via KCNJ10 channels into interstitial space from which it is actively pumped & cotransported into marginal cells
- The marginal cells release K+ into SM
- The K+ circulation is NOT aTRUE RECYCLING*
- Malfunctions of several K+ channels leads to perturbation of cochlear K+ homeostasis, resulting in hearing impairment

  For Ex – loss of KCNE1 & KCNQ1 gene (encodes K+ ch subunits that allow secretion of K+ from marginal cells to SM) leads to Jervell and Lange-Nielsen Syndrome chatz by Hearing Loss & Cardiac Arrhythmia

Passage of ions from Perilymph to Endolymph in SV



- The most well known genes involved in cochlear homeostasis are the ones that encode CONNEXIN Proteins
- Connexins form subunits of gap junction channels, which underlie K+ circulation networks described for supporting supporting cells of the Organ of Corti, the spiral ligament & stria vascularis
- Mutations involving Connexins 26, 30, 31 & 43 are responsible for majority of non-syndromic hereditary hearing loss

GENE	PROTEIN	PR. LOCATION	PR. FUNCTION	DISEASE
KCNE1	KCNE1	Marginal Cells	K+ Ch	Jervell/Lange-Nielsen Synd.
KCNQ1	KCNQ1	Marginal Cells	K+ Ch	Jervell/Lange-Nielsen Synd.
KCNQ4	KCNQ4	OHC's & IHC's	K+ Ch	DFNA2
GJB2	Cx26	Fibrocy. in SL & SLi Epi. on BM, I & B Cl	Gap Junction Protein	DFNB1/DFNA3
GJB6	Cx30	Fibrocy. in SL & SLi Supp Cells of OoC	Gap Junction Protein	DFNA3
GJB3	Cx31	Fibrocy. in SL & SLi Epithelia on BM	Gap Junction Protein	DFNA2, AR – nonsynd. deaf
GJB1	Cx32	Fibrocy. in SL & SLi Epithelia on BM	Gap Junction Protein	X-linked Charcot Marie-Tooth & Deafness
GJA1	Cx43	Fibrocy. in SL & SLi Epi. on BM, I & B Cl	Gap Junction Protein	AR – nonsynd. deafness
BSND	Barttin	Marginal Cells	Cl- Ch	Ty 4 Bartter's Syndrome

COCHLEAR FLUID HOMEOSTASIS

- Perilymph, Endolymph & Interstitial Fluid are 3 types of fluids found in the cochlea & its metabolic support system
- The proper ionic composition of these fluids is essential for generation of endocochlear potential
- Perilymph & Interstitial fluid have High Na+ & Low K+
- Endolymph have Low Na+ & High K+ , Low Ca++

Ionic composition of Endolymph & Perilymph

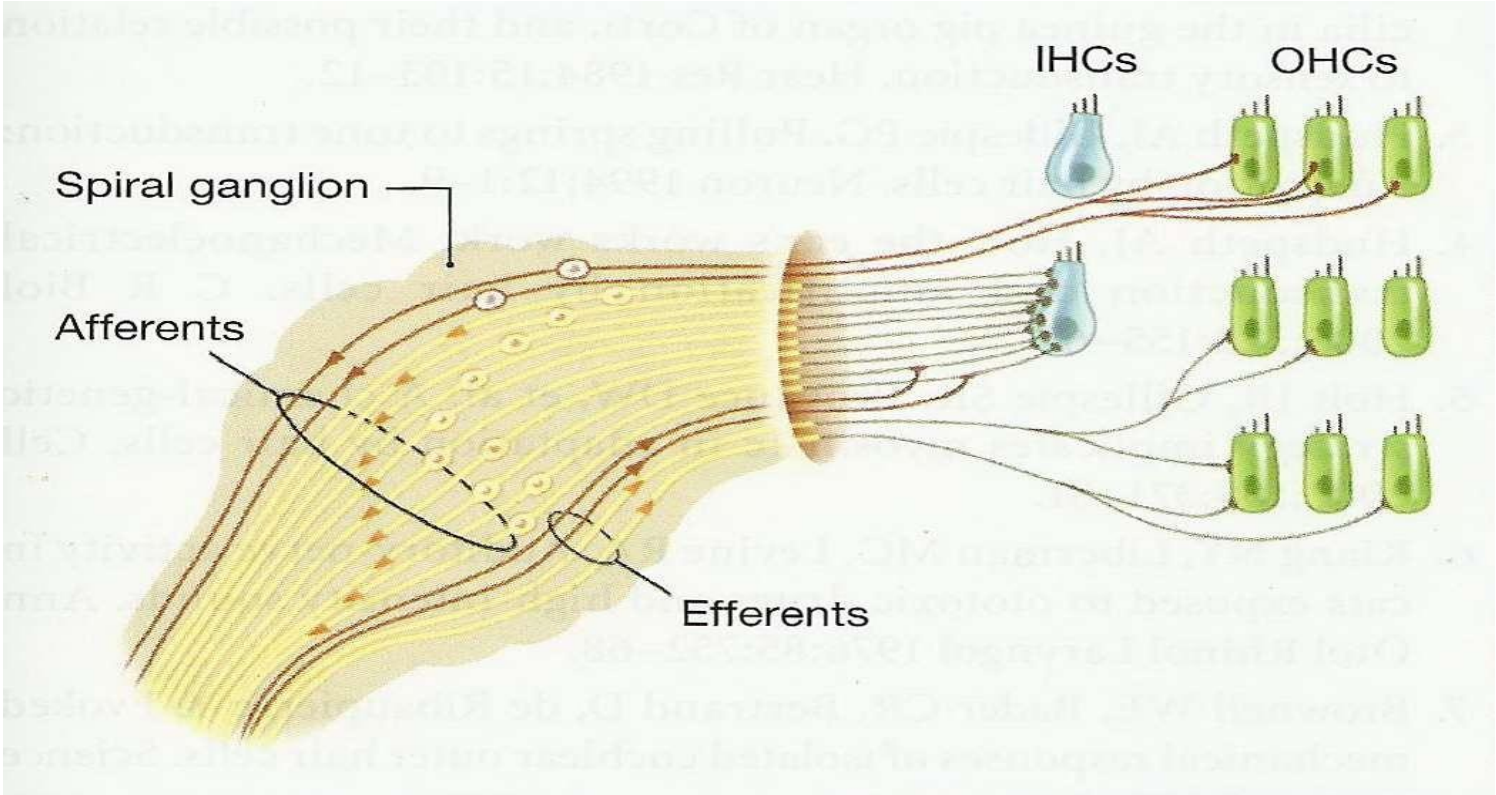
Ions	PERILYMPH	ENDOLYMPH
Na+	148	1.3
K+	4.2	157
Ca+	1.3	0.023
Cl-	119	132
HCO3-	21	31
pH	7.3	7.5

- In stria vascularis , influx of Na+ accompanies K+ from the interstitial compartment into marginal cells
- Cotransporter NKCC1 uses strong Na+ gradient to bring Na+, K+ & 2Cl- ions into marginal cells
- Na+/K+ ATPase sets up this gradient by by pumping Na+ into intrastrial space in exchange for K+
- Lastly, K+ leaves marginal cells to enter endolymphatic space
- This process maintains a High Na+ & Low K+ concerntration of intrastrial fluid, which facilitates K+ replenishment into intrastrial space

- Cl- is transported back to intrastrial space by CIC-K/Barttin Channels
- Inhibition of NKCC1 & Na+/K+ ATPase by Loop Diuretic Furosemide & Ouabain leads to supression of E-C Potential
- Mut. of Barttin gene or Mut. of both CIC-Ka & CIC-Kb subunits of basolateral Cl- Ch. leads to Bartter's Synd Ty 4 chatz by Deafness & Renal salt wasting
- Na+ is reabsorbed from endolymph by outer sulcus & Reissner's Memb cells, which play a role in maintaining Low Na+ conc of SM

- Ca++ regulation – the tip-links break at very low Ca++ conc. & the mechanoelectical transduction channels are blocked at high Ca++ concerntrations
- Ca++ carries part of transduction current & plays critical roles in Adaptation & Cochlear Amplification
- Ca++ permeable channels – Ca++ ATPases & Na+/K+ exchangers are also found & regulate Ca++ efflux & influx into Endolymph

Spiral ganglion innervations



Thank You