Musculoskeletal Physiology :

(I) Physiology of Excitable Tissues : Nerve and Muscle
(namely Skeletal Muscle)

(II) Physiology of Bone , Cartilage & Joints

Dr Taha Sadig Ahmed
Physiology Department , College of Medicine ,
King Saud University

Excitable Tissue Resting Membrane Potential (RMP)

Excitable tissues & Membrane Potential

- What are Excitable tissues ?
- Why are they denoted " excitable " ?
- What is the membrane potential (MP) ?

What are the states of MP in excitable tissues ?

- The membrane potential (MP) of excitable tissues (nerve and muscle) can be in one of 3 states :
- (1) Resting Membrane Potential (RMP) : occurs in a resting nerve or muscle cell , which is not excited by an external stimulus .
- Q : What is the range value of RMP in different nerves & skeletal muscles ?
- Answer : -70 to -90 mV (as measured in different laboratories , but not outside this range .
- In all our discussions → the -ve or +ve sign refers to the inside of the membrane .
- If the cell is excited , the RPMP changes to either →
- (2) Local Response , or
- (3) Action potential , AP. In nerves , the AP is also called Nerve Impulse

what is the difference between Local Response and action Potential ? (1)

Local Response :

Is →

(a) Graded (varies with the strength of the applied stimulus , does not obey All-or-None Law)

(b) Can be summated (the responses to a second , third , fourth or more stimuli can be added on top of the response to the first stimulus)

(c) Non-propagated : this electrical change can be measured only in the membrane area close to the stimulation point ‘ & it gradually fades as we go away from the stimulation site . It does not get conducted (propagated) all the way along the nerve .

what is the difference between Local Response and action Potential ? (2)

Action Potential

Is →

(a) It is not graded → Obeys All-or-None Law .

(b) APs are electrical potentials that do not summate .

(c) APs are propagated (conducted) all the way along the nerve to its terminal

- At the peak of the AP , the value of the MP reaches

  +35 to +40 mV
- In nerves , the AP is generated at the Axon Hillock
- By contrast , a local responses can be generated at any membrane area if the stimulation is sufficient .

More About Local Response (1)

- In case of local responses :
- (a) If the stimulation is excitatory (opening sodium or calcium channels) , it produces a depolarizing local response → which makes the inner side of the membrane less negative

  (i.e., reduces the numerical value of the RMP)
- (b) If the stimulation is inhibitory (opening potassium or chloride channels) , it produces a hyperpolarizing local response → which makes the inner side of the membrane more negative (increases the numerical value of the RMP) .

More About Local Response (2)

- At synapses , where neurotransmitters mediate opening of channels , (a) mentioned in previous slide is called → Excitatory Postsynaptic Potential (EPSP) ,
- and (b) is called Inhibitory Postsynaptic Potential (IPSP) .

Now , going back to the unique property of excitable tissues :

- Q: what makes them different from other body tissues ?
- A: Their membrane acts as an electric capacitor , storing opposite charges on the opposite sides of the membrane : this creates a RMP of high value (-70 to -90 mV) compared to other body cells (in RBC , for example , MP
  is around -5 mV) .
- This high RMP makes the cell-membrane function as a capacitor , that can "discharge" , producing large voltage changes (action potentials) if its sodium or calcium ionic channels are opened .
- This is because opening of these channels tends to " depolarize " the cell .

Q: What are the types of membrane ionic channels ?

- (1) Leak (Diffusion , Passive) channels: are pores in the cell-membrane which are open all the time , therefore ions diffuse through them according to the ion Concentration Gradient .
- Because the concentration of sodium outside the cell is more than inside , the direction of the Na^+ chemical (concentration gradient) gradient is inward → and sodium continuously diffuses through the Na^+ leak channels from outside (the extracellular fluid , ECF) to inside the cell (the intracellular fluid , ICF).
- On the other hand , because the concentration of K^+ is higher inside the cell than outsideF → therefore potassium continuously diffuses through the K^+ leak channels from inside the cell to outside .
- (2) Voltage-gated channels : open when the cell-membrane is electrically activated .
- (3) Chemically-gated (ligand-gated) channels : opened by neurotransmitters at synapses .

Na+ Nernst (Equilibrium) Potential

- The cell-membrane is practically considered as a semi-permeable membrane separating the ECF from the ICF .
- Nernst made a hypothesis which was later verified mathematically as well as in the physics laboratory under artificial conditions .
- Nernst , hypothetically speaking, said that if we suppose that (1) the ECF and ICF contained ONLY sodium ion , (2) and that the cell-membrane was freely permeable to Na+ :
- → then Na+ will diffuse down its concentration gradient to the I nside of the cell, carrying with it +ve charges , and progressively decreasing the negativity on the inner side of the membrane .
- As this goes on and on , and as the positive charges build inside , an opposing Electrical Potential begins to develop , tending to prevent the +ve Na+ from entering.
- This electrical potential will grow until it becomes strong enough to balance and counteract the concentration gradient which tends to push Na+ inside .
- When this electrical gradient (force) , which tends to drive Na+ outside = the concentration gradient (which tends to push Na+ in) → there will be no net Na+ movement across the membrane .
- The MP potential in that case is called Nernst Potential for Na+ (or Na+ Equilibrium or Diffusion Potential) = +61 mV .
- (The charge always refers to the inside of the cell) .

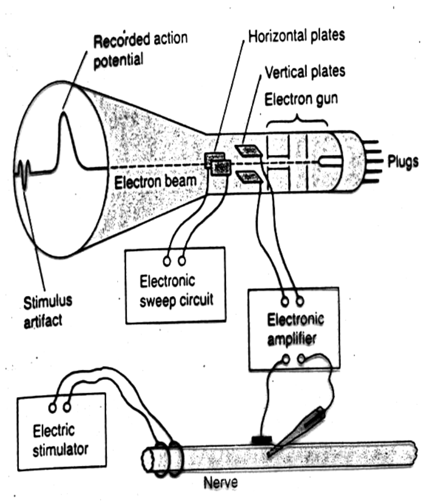
The Potassium Nernst (Equilibrium) potential

- Similarly , (1) if the ECF and ICF contained <u>ONLY</u> potassium ions (2) and the membrane was freely permeable to K+
- → then K+ will diffuse down its concentration gradient (via the K+ leak channels) from inside the cell to outside , carrying with it +ve charges to the outside , thereby progressively increasing the negativity on the inner side of the membrane (because we are losing +ve charges from inside).
- At this goes on and on , and as negative charges build inside , an opposing electrical potential begins to develop , tending to prevent the exit of the +ve potassium ions .
- This electrical potential will grow until it becomes strong enough to balance and counteract the concentration gradient which tends to push K+ outsude
- When this electrical gradient (force) , which tends to keep K+ inside = the concentration gradient (which tends to push K+ outside) → there will be no net K+ movement across the membrane .
- The MP potential in that case is called Nernst Potential for K+ (or K+ Equilibrium or Diffusion Potential) = -94 mV .
- (The charge always refers to the inside of the cell relative to the outside)

- <u>What determines the magnitude (value) of the Equilibrium (Nernst) Potential ?</u> The <u>ratio</u> of the ion concentration on the two sides of the membrane .
- <u>How can we determine the value of this Nernst (Equilibrium) Potential for a given ion (sodium or potassium) ?</u>
- The value of this potential EMF can be determined by one of 2 ways :
- (1) It can be calculated using Nernst equation and the concentration of the ion →
- Nernst Potential (mV) = +/- 61 log Conc inside/Conc outside
- (2) Or, alternatively , it can be measured directly in the laboratory using electrodes (see next slide)
- The value of the Nernst Potential for K+ = -94 mV
- The value of the Nernst Potential for Na+ = +61 mV

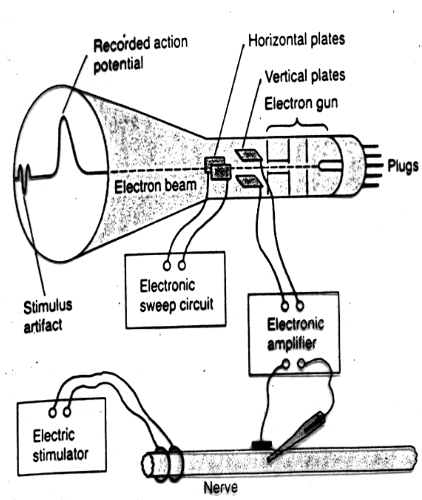
Measurement of MP Using Intracellular Electrode (1)

- Two electrodes are used : an intracellular " active electrode "and an extracellular " reference " (also called , or inactive or indifferent) electrode .
- They are connected amplifier and a cathode-Ray Oscilloscope (CRO) .
- Under artificial laboratory conditions one ion will be in the medium (sodium or potassium) to measure its Equilibrium (Nernst) potential .
- This will give +61 mV in case of sodium & -94 mV in case of potassium .
- However , in real life we have both sodium & potassium , in addition to chloride (which does not contribute much to the RMP) in the extracellular fluid .
- In that case we will be measuring the RMP , which will be -70 to -90 mV (as measured in different laboratories & in different excitable tissue cells)

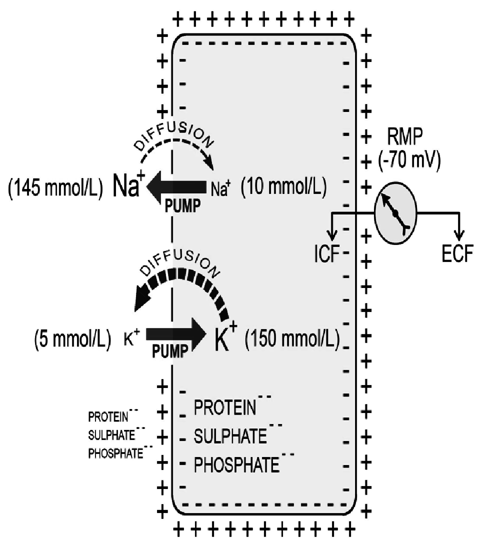


Measurement of MP Using Intracellular Electrode (2)

- However , in real life situation we have both sodium & potassium , in addition to chloride (which does not contribute much to the RMP) in the extracellular fluid .
- In that case we will be measuring the RMP , which will be -70 to -90 mV (as measured in different laboratories & in different excitable tissue cells)
- If we use an electric stimulator to stimulate the nerve to threshold → we get an AP → & the measred MP will change to have a peak of + 35 to + 40 mV

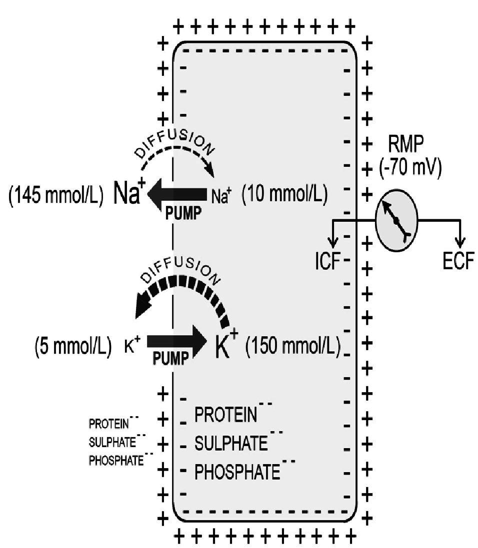


Origin of the RMP (1)



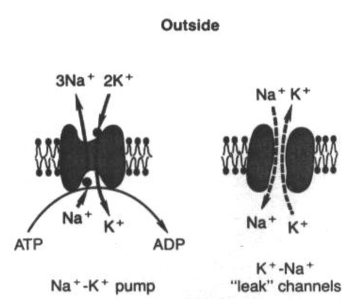
- Two questions should be asked :
- Q1: What are the factors that make the inside of the cell negative ?
- Q2: and give the RMP the value of -70 to -90 mV ?
- Answer to both questions : the 3 factors are →
- (1) At rest , K+ leak channels are more effective than Na+ leak channels → more K+ diffuses to outside than Na+ to inside → i.e , the membrane is 50 -100 times more permeable to K+ than to Na+ →more potassiumlost than sodiumgained → net loss of +ve ions from inside the cell → more negative inside

Origin of the RMP (2)



(2) Large intracellular anions (proteins , sulphates & phosphates)

(3) The sodium-potassium pump (3Na+ pumped out in exchange for 2 K+ pumped in) → net loss of +ve ions



- Thus in a resting cell , the RMP is closer to the potassium equilibrium potential than to sodium equilibrium potential i.e., potassium has the upper hand .
- Therefore , we can say that the RMP depencds mainly on difference in concentration of potassium inside & ouside the cell
- Whereas , as we will see later , the value of the MP during the Ap depends mainly on difference in concentration of sodium inside & ouside the cell i.e., during the AP sodium has the upper hand
- Q : What is the effect of increasing extracellular potassium concentration on the RMP ?

- End of L1