Bio3411
Midterm Review

Oct 24/25 2005
Ben Kolber

Lecture II

- Gray versus white matter
- Parts of the neuron (axon, dendrites etc)
- Categories of glia
  - Astrocytes, microglia, oligodendrocytes, Schwann cells
- Parallel Processing by the brain (compared to serial processing by a computer)
  - BUT neuron/brains still act like a computer because they integrate information
Lecture III-IV

- Introduction to the neuron as a battery
  - Unequal distribution of ions makes a neuron a battery
    - Maintained by Donnan Equilibrium and Na/K ATPase
    - Chemical vs Electrical gradient
      - Electrical force greater than chemical (means that during an AP no detectable change in Bulk ion concentration)
  - Length Constant
    - \( \lambda = \sqrt{\frac{R_m}{R_i}} \)
    - Increased (in organisms) by increasing \( R_m \) (myelination) or decreasing \( R_i \) (increasing axon diameter)

Lecture III-IV

- Passive vs Active propagation
  - Passive involves one battery and ions bumping into eachother
    - Involved in moving AP through myelinated parts of axon
    - Involved in the initial depolarization of axon to threshold
  - Active involves many batteries (system regenerates), ions flowing across membranes
    - Occurs at Nodes of Ranvier

- Permeability (P)
  - Ability of an ion to move across membrane
  - Similar (although not mathematically identical) to conductance (g)
Lectures IV-V

Potential (V)
- For Cell - resting potential $V_m$ or $E_m$
  - Potential at which there is no net current for all ions
  - Determined with Goldman equation (permeabilities) or “Salkoff” equation (conductances)
- For each ion - equilibrium potential $E_{ion}$ (eg $E_{na}$)
  - Nernst equation $E_{ion} = \frac{58/z}{log ([ion]_out/[ion]_in)}$
  - Potential at which there is no net current for a single ion
- For each non-selective channel - reversal potential $E_{rev}$
  - Potential at which there is no net current flow through a channel
  - For a channel with equal conductances (g) for K and Na, $E_{rev}$ is also the point at which $DF_{Na} = DF_{K}$

Lectures IV-V

Know ion concentrations and equilibrium potentials

<table>
<thead>
<tr>
<th></th>
<th>Na+</th>
<th>K+</th>
<th>Cl-</th>
<th>Ca++</th>
</tr>
</thead>
<tbody>
<tr>
<td>Out (mM)</td>
<td>145</td>
<td>5</td>
<td>110</td>
<td>1-2</td>
</tr>
<tr>
<td>In (mM)</td>
<td>5-15</td>
<td>145</td>
<td>~20</td>
<td>~&lt;.001</td>
</tr>
<tr>
<td>$E_{ion}$ (mV)</td>
<td>57-85</td>
<td>-85</td>
<td>-43</td>
<td>124</td>
</tr>
</tbody>
</table>
Lectures V-VI

- Driving force (actually lecture VII)
  - Force pushing a type of ion across the membrane to move the membrane potential to $E_{ion}$
  - $DF_{ion} = V_m - E_{ion}$
  - Relationship between two ions when membrane voltage is constant (no net current)
    - $g_{ion1} \times DF_{ion1} = -(g_{ion2} \times DF_{ion2})$

Lecture VI

- Channel States
  - closed ↔ open ↔ inactivated

- Voltage sensor (pos. charged aa’s in S4 TM loop)
- Pore (“P” loop) - Uses size and chemical interactions to exclude/include ions
  - Chemical interactions between aa’s and ion mimic ion’s waters of hydration
Action Potential

Know the parts of the “normal” action potential including the channels involved
- At rest, leak K channels dominate (although leak Na channels are open)
- Depolarization by voltage-gated Na channels (which then inactivate from peak to start of undershoot)
- Repolarization by voltage-gated K channels
- Undershoot
  - V-K channels cause undershoot which ends when V-K channels close
  - Return from undershoot occurs because of Na ions flowing into the cell through Na leak channels (and somewhat because of the Na/K ATPase)

---

Action Potential

Refractory Period
- Total = absolute + relative
- Absolute - All V-Na channels are inactivated and so you CANNOT fire an AP
- Relative - When the potential is hyperpolarized (relative to resting potential) as seen during the undershoot
  - Requires larger stimulus to reach threshold and fire an AP
  - Threshold actually CHANGES during undershoot
Cardiac Action Potential

- Know the role of Voltage-gated Ca\(^{++}\) channels in prolonging AP
  - What other channels are involved in the cardiac AP?

<table>
<thead>
<tr>
<th>Normal ventricular AP</th>
</tr>
</thead>
<tbody>
<tr>
<td>V-Na channels</td>
</tr>
<tr>
<td>V-Ca channels</td>
</tr>
<tr>
<td>KQT channels</td>
</tr>
<tr>
<td>HERG channels</td>
</tr>
</tbody>
</table>

K\(^{+}\) Channelopathies

- Major types/groups/families of K\(^{+}\) channels
- Shaker mutation (in comparison to normal Shaker K channel)
  - Normal - repolarization of motor neuron
  - Mutation - change in refractory period causes Episodic Ataxia
- Slo Channel (voltage and Ca gated)
  - Normally repolarize presynaptic membrane
- CNG (not voltage gated)
  - Gated by cyclic nucleotides
  - Involved in starting AP at sensory nerve endings
- SK (not voltage gated, Ca++ gated)
  - Increases duration of undershoot
**Channelopathies (cont.)**

- KQT K+ Channels (aka KCNQ)
  - Normally repolarize cells
  - Mutation increase AP length and causes LQT (cardiac) and BFNC (CNS)
- HERG K+ Channels (eag family)
  - Strange K+ channel with 3 states - closed to inactivated to open
  - Involved in cardiac AP repolarization
  - Mutation causes LQT (cardiac)
- Hyperkalaemia Paralysis
  - Important feature of hyperkalemia is an increase in $V_{rest}$
  - Leaky V-Na channel in muscles

**Synaptic Transmission**

- Neurotransmitters
- Synaptic Release
- Synaptic Plasticity
Neurotransmitters

- Acetylcholine (found at NMJ and other places)
  - Nicotinic receptors (channels) and muscarinic receptors (GPCRs)
- Inhibitory
  - GABA and glycine
- Excitatory
  - Glutamate
    - AMPA, NMDA metabotropic receptors
  - Dopamine, norepinephrine etc
    - Metabotropic receptors
  - Peptide NTs
    - Metabotropic receptors

Neurotransmitter Receptors

- Ionotropic
  - Ion channel, often non-selective, has a reversal potential
- Metabotropic
  - Main receptors for neuropeptides
  - GPCR
  - Understand B-adrenergic signaling (G_{as} increases cAMP and PKA) and metabotropic Glu signaling (G_{aq} increase PKC and Ca++) pathways
Short Term Plasticity

- Occurs because of presynaptic events
- Summation
  - Spatial or temporal
  - Multiple APs causes additive PSP response
  - Can include EPSP and IPSP
- Facilitation
  - Repetitive stimulation
    - Buildup in presynaptic Ca++ from multiple APs in one presynaptic cell
  - Presynaptic
    - Buildup in presynaptic Ca++ from prolonged presynaptic depolarization (because of input from a presynaptic facilitating interneuron)

Long-term plasticity

- Occurs b/c of postsynaptic changes
- LTP - Increase in EPSP after an intense tetanus stimulation
  - Ca++ in postsynapse activates protein that ADD AMPARs into membrane
- LTD - Decrease in EPSP after an long low frequency stimulation
  - Ca++ in postsynapse activates proteins that REMOVE AMPARs from membrane
Immune Diseases

- Multiple Sclerosis (MS)
  - Antibodies against MBP (CNS myelin)
    - Slows AP velocity; injures axons
  - Mainly CNS disorder
  - Motor weakness, visual problems, sensory deficits etc

- Antibodies against channels
  - Myasthenia Gravis
    - Autoantibodies against nAChRs
    - Exercise induced muscle weakness
      - Repetitive stimulation of NMJ decreases an already reduced EPP
    - Treated with anticholinesterase drugs or immunosuppressants
  - Rasmussen’s encephalitis
    - Abs against AMPA subunit (R3)
      - Abs mimic glutamate causing excitation
    - Disease confined to one hemisphere
    - Mysteries:
      - Why is it confined to 1 hemisphere?
      - How do the Abs get into brain?
Toxins

- Conus (from cone snail)
  - Target multiple families of ion channels
- Bungarotoxin
  - Binds to nAChRs irreversibly
- Dendrotoxin (blocks K channels)
- Charybdotoxins (blocks K channels)
- Apamine (blocks SK channels)

K/Na conductances in Squid action potential
- TTX (tetrodotoxin) - blocks Na channels
- TEA (tetraethylammonium) - blocks K channels
  - Charybdotoxin (CTX) very similar
- Saxitoxin (same action as TTX)
- Curare (blocks nAChRs in periphery)
- Strychine (blocks glycine Rs)
- Picrotoxin (blocks GABARs)