review session: Sun. afternoon 3pm

(spiral cord) preganglionic postganglionic
inputs outputs
(1 synaptic layer)

-in Aplysia, Kandel etc. looked for changes in presynaptic cell (b/c sensitization → lower m...?)
-can’t record from presynaptic terminal, so looked in cell body

record

sensory neuron

higher (lower Po)

↑ tickle gill
-tickling cell gives AP
-after sensitization or applying 5-HT,
AP can turn broader

↑↑ with 5-HT or sensitization

(spike broadening)
(even broader: if block Ca²⁺ channels)

- Spike broadening consequence of cAMP?

- cAMP binds 2 sites on R, releases C, can go phosphorylate stuff

- Kandel et al injected:
  1. catalytic subunit (got spike broadening)
  2. superregulatory protein (“Walsh inhibitor”): regulatory subunit w/ no cAMP-binding sites;
     constitutively turns off PKA (this protein is PKI)

- Injecting PKI blocks spike broadening & synaptic effect (potentiation)

- PKA can phosphorylate channel: activate depolarizing or inactivate hyperpolarizing channel
- found that K⁺ channel inactivated
- Patch-clamped sensory neuron, pulled off patch (w/ channels): cytoplasmic face outside
- Applied voltage ramp, found noise (in 2, 3, 4 quadrants): 4 channels on membrane, patch, open most of time
- Apply catalytic PKA subunit, get average of 1-2 channels, get recovery (quicker if treat w/ phosphatase)
- K+ channel tried to keep membrane repolarized (K+ S channel); PKA phosphatase + closer, lose some repolarizing K+ current during AP, get spike broadening
- Broadening AP keeps cell depolarized longer, more Ca2+ influx, more transmitter release

If touch one part of gill, give tail shock, touch another part w/ no tail shock, both parts sensitized
- Pairing = specific component on top of general sensitization, however

- Can take identified abdominal ganglion neuron (sensory & motor), just cell bodies, need serotoninergic neuron too to apply low 5-HT, make other two types grow, get synapses
- Applying 5-HT gives synaptic facilitation in dish as well as in animal
- Usually last 10-20 minutes
- If apply 5-HT pulse ~1 minute apart, get synaptic facilitation that lasts 2-4 hours:
  - Long-term memory in dish
  - Block long-term memory w/ inhibitors of transcription & translation (doesn't block short-term form)
  - Long-term synaptic facilitation requires protein synthesis
  - CREB transcription factor regulates gene expression downstream of cAMP

Anti-
- Inject CREB (Aplysia) into nucleus of sensory neuron, blocks synaptic facilitation
  *4Mediated by this transcription factor
  (This is also true in mice & flies: blocking CREB gets rid of long-term memory)

Sensitization = general increase in responsiveness after strong or noxious sensory stimulus
  (eg chip screaming or poking gill w/ electricity)
classical conditioning:
- stimulus like bell (normally no response) (CS)
- pair bell w/ food: training
  4. normally gives salivation (US) (or reinforcement): food is positive reinforcement
- testing afterwards, bell alone gives salivation
  4. trained responsive specific to paired cue: must be sound-off this bell

bell sound
- go to auditory cortex, pathway
- go to similar premotor cells
- must be latent connection between ear & deal (no time to forge new connection)

food goes to visual cortex?
- pathway goes to premotor cells, gives you deal reflex

synapse A always excitatory: boring
- constitutively excitatory

synapse B is Hebbian synapse
- initially ineffective (no deal)
- strengthened by paired training,
  eventually sound alone gives deal
- want synapse to become synaptically detector
  strengthened if presynaptic & postsynaptic cells fire together

"cells that fire together wire together"

Hebb found simplest synapse that shows this
- initially no effect at synapse
  more & more firing together = more strengthening of synapse

HM = bilateral medial temporal lobe lesions, including hippocampus
- need hippocampus to store a class of memories
- hippocampus curdled, "sea more"
- circuit is simple (trisynaptic)
  post-synaptic inputs:
  Schaffer collaterals
  perforant pathway
  parietal lobe pathway
  CA3
  pyramidal cells
  CA1
  dentate granule cells
- Mouse hippocampus has same neuroanatomy as human

- Hippocampal defects: can't recognize new faces, remember events
  - In mouse, test w/ Morris water maze (pool, circular, full of opaque liquid, w/ hidden platform; mouse will swim until finds hidden platform)
  - Can train mouse to know where platform is, w/ external room cues to navigate
    - Removal of hippocampus removes this ability

- Stimulation Schaffer collateral, record intracellularly in postsynaptic CA1 cell:
  - Get EPSP at certain frequency
  - Give stimulus, e.g., 100 Hz; afterwards, get bigger EPSP, then goes back
    - Potentiation

- LTP in Schaffer collateral pathway

= 2 inputs 2 regions of Schaffer collateral that are separate, stimulate different fibers

- SCI stim (separate out EPSP traces)
  - SCI stimulated, SCI potentiated (specific)
  - SCA not

- Long-term potentiation is synapse-specific
  - If fire SCA during SCI tetanus, both are potentiated
    - "Cells that fire together wire together"

- Same time as tetanus
presynaptic firing during postsynaptic depolarization will give LTP (potentiation)
- no potentiation if current keeps Vm at resting during presynaptic tetanus
- cells as similarity detector: presynaptic firing l postsynaptic depolarization

- neurotransmitter used in these cells is glutamate
  - 2 interesting types of 6kRs on postsynaptic membrane:
    - 1. AMPA R: antagonist
      - agonist (CNQX), agonist = AMPA
    - 2. NMDA R: antagonist (APV or AP5), agonist = NMDA

- applying CNQX blocks almost all synaptic transmission
- AMPA R conducts 95% of inward excitatory current in EPSP
- applying APV blocks only 5% of EPSP, but blocks LTP almost completely

- AMPA Rs conduct Na⁺ (almost purely)
- NMDA Rs conduct Na⁺ + Ca²⁺

- synaptic plasticity depends on NMDA Rs
  - l² ligand-gated channel opened by glutamate (and antagonist agonist NMDA)
  - unless depolarized, Mg²⁺ will block channel, no Ca²⁺ influx
  - this channel itself is Hebbian similarity detector: need presynaptic activity (↑ glu)
    and postsynaptic activity (depolarization of Vm) to open, let in Ca²⁺
    (with Mg²⁺, don't need depolarization for Ca²⁺ conductance)