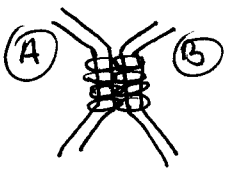
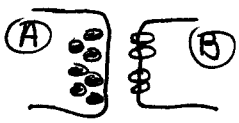
NEUROBIOLOGY
SYNAPSE IIA

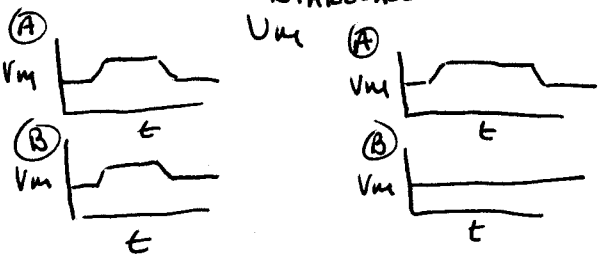
ELECTRICAL



CHEMICAL

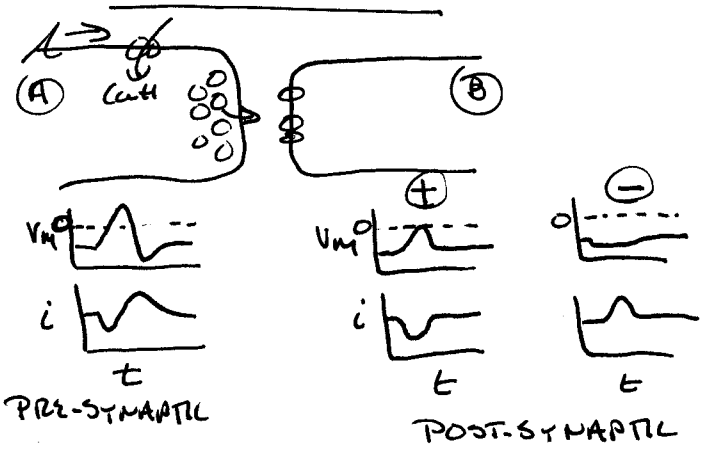


SUBTHRESHOLD V_m



INJECT CURRENT IN (A)
MEASURE V_m IN (A) & (B)

CHEMICAL SYNAPSE



PRE-SYNAPTIC

POST-SYNAPTIC

Fatt, Katz, Eccles, Kuffler 1941, 1951, 52

(CURARE) EPPs - END PLATE POTENTIALS
(POST SYNAPTIC POTENTIALS = PSPs)

MEPPs - MINIATURE EPP (MPSPs)
[CHANCE OBSERVATION!

del Castillo & Katz (~~1954~~) (1954b)
1:1 Relationship between MPSP & QUANTA

MPSPs HAVE UNIT HEIGHT/AMPLITUDE

MPSP ARE QUANTAL RESPONSES TO PACKETS OF ACh (NEUROTRANSMITTER)

QUANTAL RELEASE
QUANTIFYING QUANTA

also - del Castillo & Katz (1954a)

Ca^{++} & Mg^{++} antagonistic on ACh release

Ca^{++} ⇒ ACh release

Ca^{++} + Mg^{++} ⇒ inhibit ACh release

effect of Mg^{++} countered by increasing $[Ca^{++}]$

Mg^{++} competes w/ Ca^{++} at some Ca^{++} binding site

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del Castillo & Katz 1954b

MEPPs - small "all or none" units
0.5 - 1.0 mV

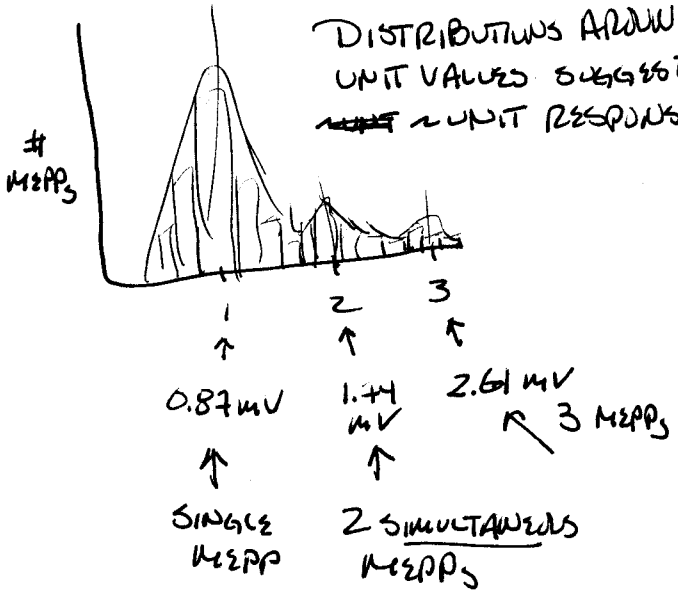
EPP ~ 70 - 80 mV

[BLOCK AP by REDUCING MEPP # w/ Mg^{++} (CONTROL ACh)]

Hypothesis: MEPPs are responses to "parcels of ACh"

Q: IS NORMAL EPP "MADE UP IN THIS QUANTAL FASHION"

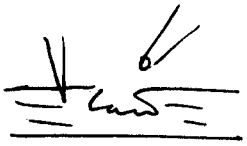
COUNT MEPPs - MEASURE AMPLITUDES



DISTRIBUTIONS AROUND UNIT VALUES SUGGEST ~~NOT~~ ~ UNIT RESPONSE

How much ACh in Quantum?

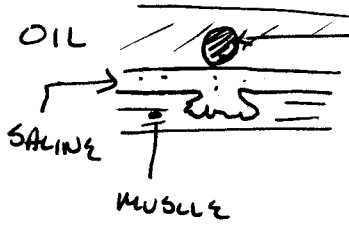
Kuffler & Yoshikami (1975b)



"puff" ACh onto endplate w/ axon removed

What size "puff" = MEPP size depolarization?

① - Calibrate puff



Water "droplet" in oil - 0.6nl

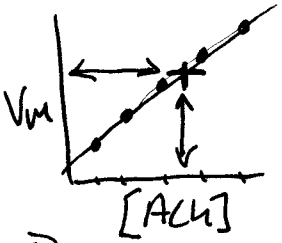
Specific [ACh] concentrations

Drag to oil-saline interface - pops open

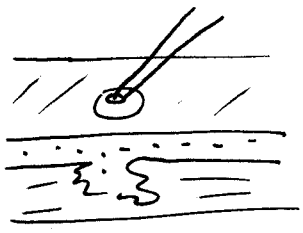
Dumping contents onto muscle - POW!

Measure response

Make "standard curve"



② Make 0.6nl droplet using ACh pipette (pump out ACh using current)



In their study

A 0.6nl ejection = some amplitude response

Compare to standard curve

Determine # ACh molecules

30,000 molecules / pL

pico coulomb unit of charge used to pump ACh out of pipette

~~6000~~ 5mV response / pL

∴ 6000 molecules / mV

Estimate 1 MEPP < 10,000 molecules (upper limit)

Further - is quantum = vesicle?

1984: vesicles - 40-50 nM dia.

10000 molecules per 40-50nM vesicle = 260-505 mM

Close ~ isosmotic

Saline ~ 320 mOsm

K&Y (1975b) noted that, in 1966, Sheridan et al showed that contents of presynaptic vesicles in the electric fish Torpedo were isosmotic with the fish plasma, supporting their estimations (above).

∴ - yes, perhaps, vesicle does = quantum

Hurlbut et al 1990

Control production of MEPPs using Ca^{++} free medium (no NT release) + either black widow spider toxin (releases NT) or α-latrotoxin + Mg^{++} (also releases NT)

⇒ correlate # MEPPs (measure V_m) w/ # lost vesicles (use electron microscope to look)

1:1 relationship

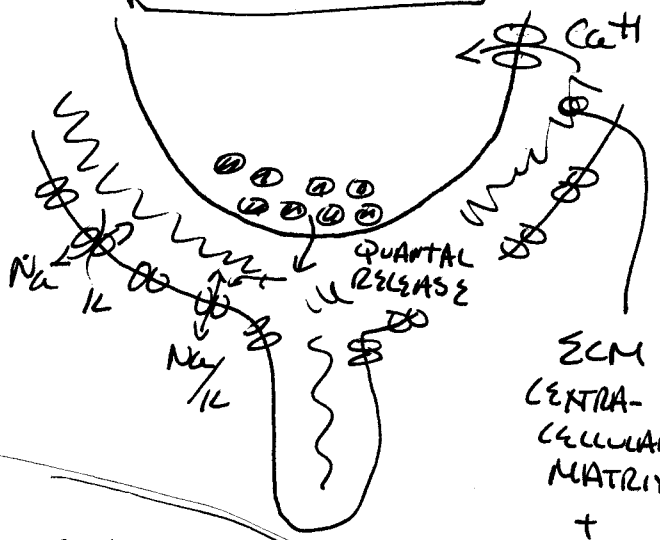
∴ 1990 - yes

Vesicle = quanta

~ 1 vesicle / MEPP

Hurlbut et al. actually conclude with a more conservative position, stating that their results suggest at least that a quantum is 1-2 vesicles, and not 7-10 vesicles as others had recently been suggesting.

MUSINGS ON #5



Ca^{++} INDUCES INCREASE IN VESICLE RELEASE

FROM BOOK (Nicholls etal)

ACh RECEPTOR/CHANNEL

30pS/channel

40-50nS/MEPP

∴ ~1300 CHANNELS/MEPP

2 ACh molecules required to activate 1 RECEPTOR

∴ 1300 CHANNELS = 2600 ACh MOLECULES

"SPONTANEOUS MEPPs" MEANS VESICLES ALWAYS RELEASED. Ca^{++} COORDINATES LARGE SYNCHRONOUS RELEASE ⇒ EPP

(ALSO BACKGROUND LEAKAGE OF NON-VESICLE ACh FROM CYTOPLASM)

5-10K ACh/QUANTUM ⇒ 1300 CHANNELS @ 2 ACh/ch

nS/pS = NANO/PICO SIEMAN = UNIT OF CONDUCTANCE

$S = \frac{1}{ohm}$ $e = iR$ $S = \frac{1}{R} = \frac{i}{e}$

FROM BOOK (Kandell etal)

30 pS/channel ≅ -2.7pAMP @ -90mV

FOR CHANNEL w/ MEAN OPEN TIME = 1 msec

per channel ≅ 17000 Na^+ IN, slightly fewer K^+ OUT per msec

CALCS. FOR ACh, MOTOR END PLATE LARGE SYNAPSES/LARGE CELLS

FOR SMALLER CELLS/SYNAPSES - FAR FEWER MOLECULES & RECEPTOR CHANNELS

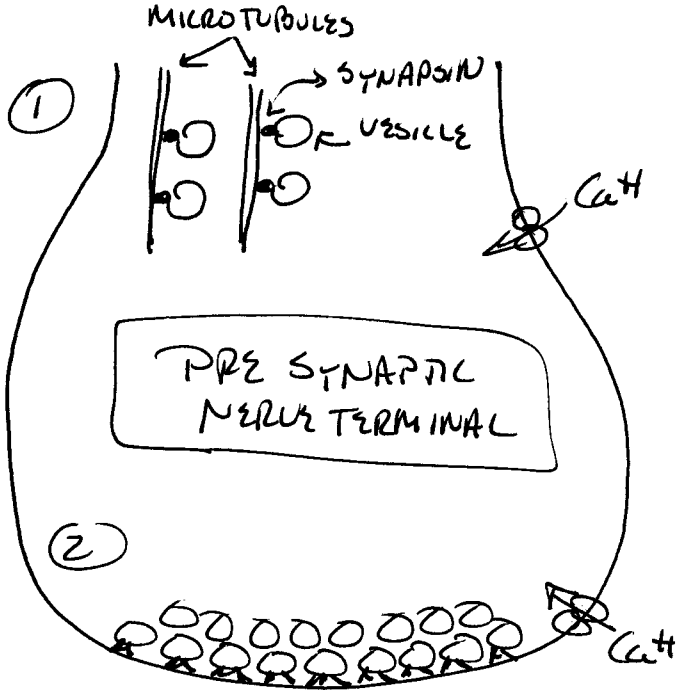
HIPPOCAMPUS - INHIBITORY SYNAPSE - 1 QUANTUM → 20 CHANNELS

ALL OF THIS EFFORT HAS FOCUSED ATTENTION ON VESICLES -

- SYNTHESIS OF NT & STORAGE IN VESICLES
- STORAGE & RELEASE OF VESICLES

ESP. IMPORTANT ⇒

- RECYCLING OF VESICLES



① STORAGE POOL OF VESICLES

BOUND TO MICROTUBULES BY "SYNAPSIN"

Ca^{++} → CALMODULIN → PK - Phosphorylate Synapsin / Release Vesicle

② RELEASE POOL OF VESICLES

FUSION PORE PROTEINS ANCHOR VESICLE TO MEMBRANE

Ca^{++} BINDS TO PROTEIN TRIGGERING RELEASE