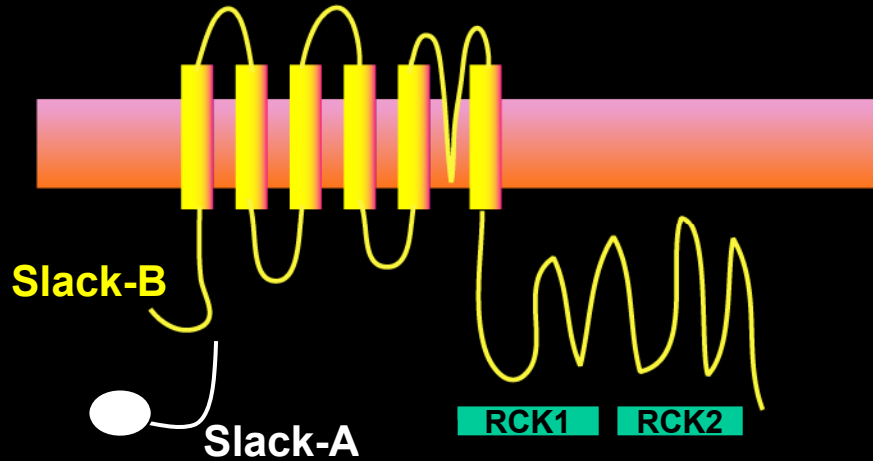


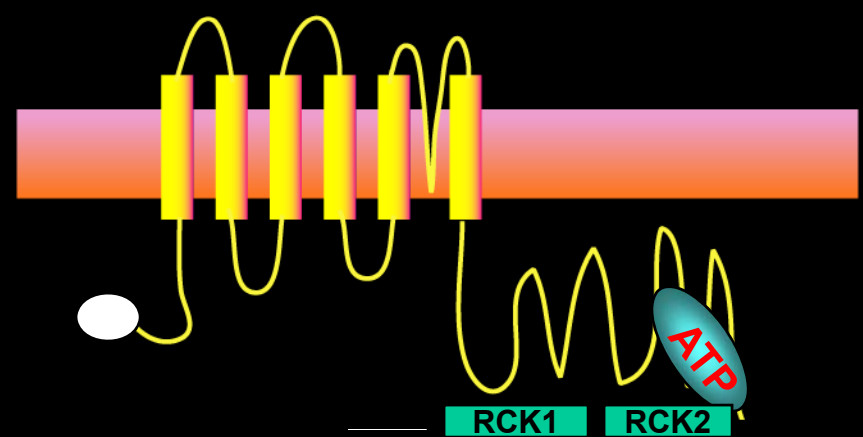


Sodium-activated potassium channels

Slack



Slick

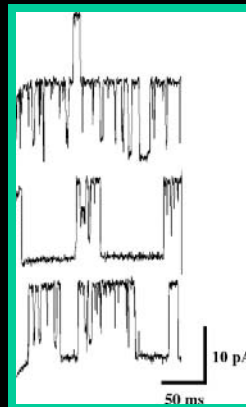
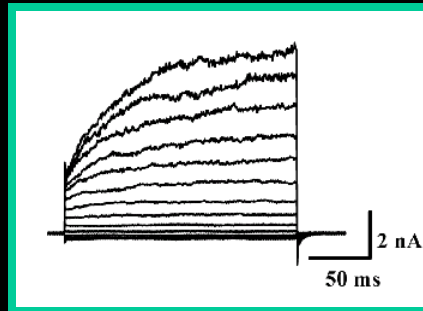


Chromosome 9q34.3
-alternative promoters

-Slow activation with voltage (Slack-B)

-Increased by PKC and mGluR activation

~180 pS



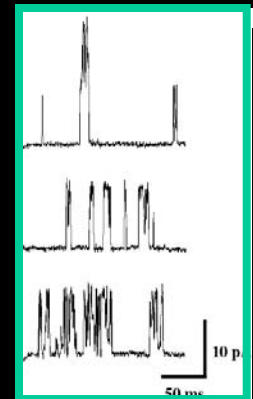
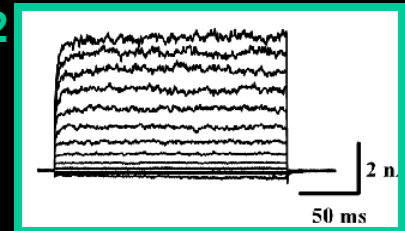
Chromosome 1q31.2

-Rapid activation with voltage
-regulated by intracellular ATP

-Decreased by and mGluR PKC activation

-activated by intracellular Cl⁻

~140 pS

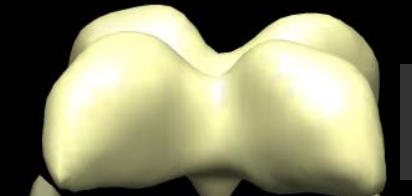


3-D Structure of Slack-B Channels

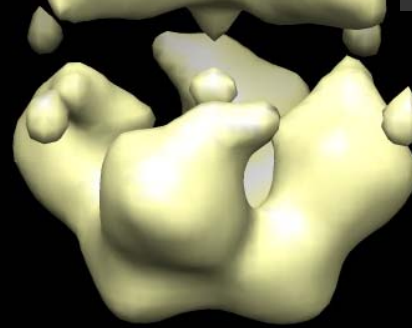
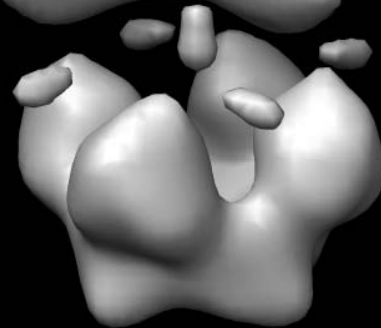
Open

Closed

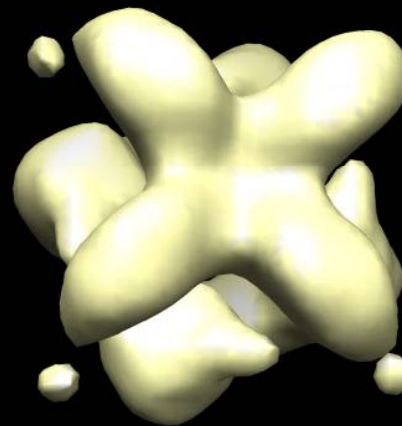
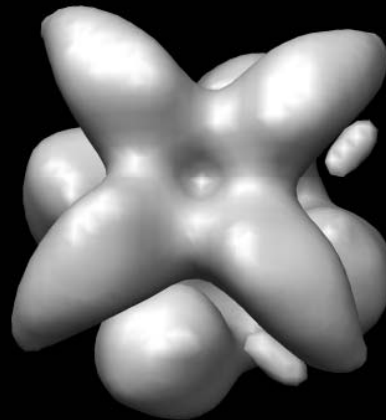
Out



In

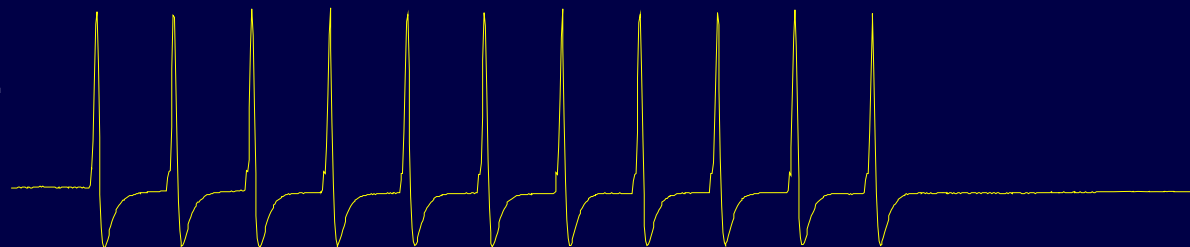


Top

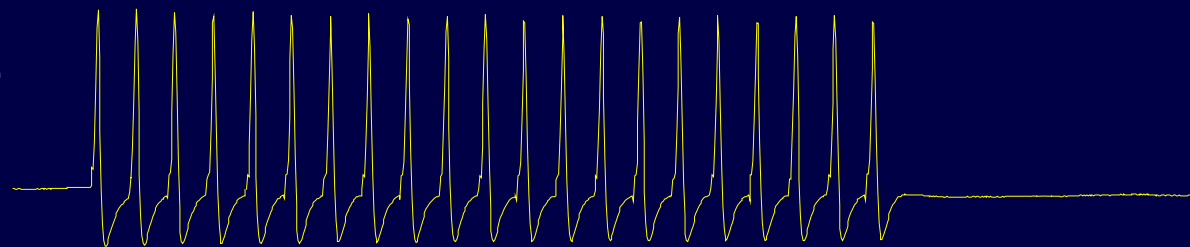


100 Å

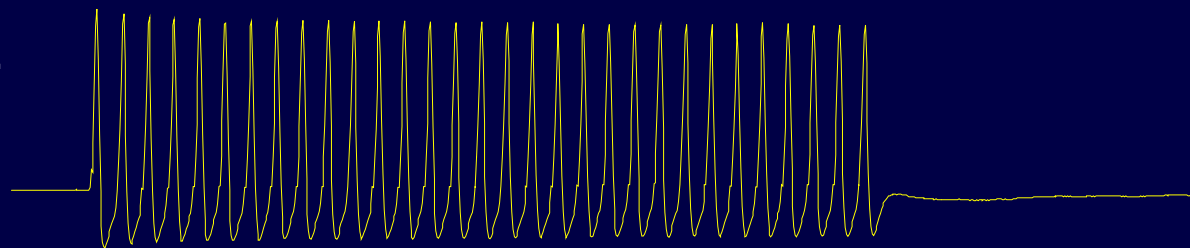
100 Hz



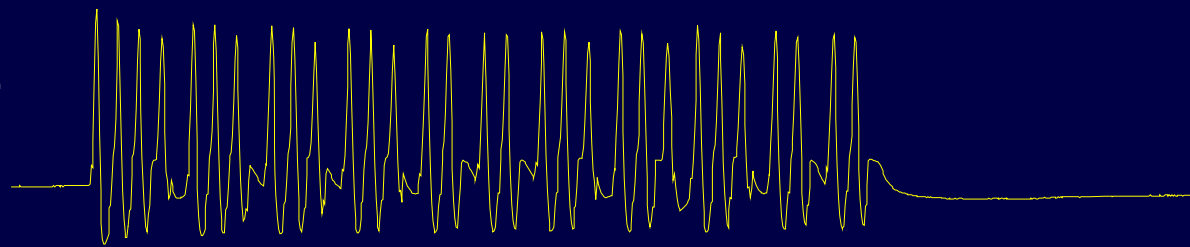
200 Hz



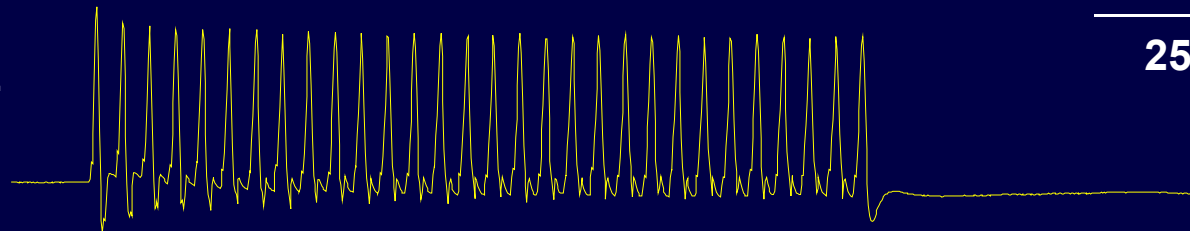
300 Hz



400 Hz



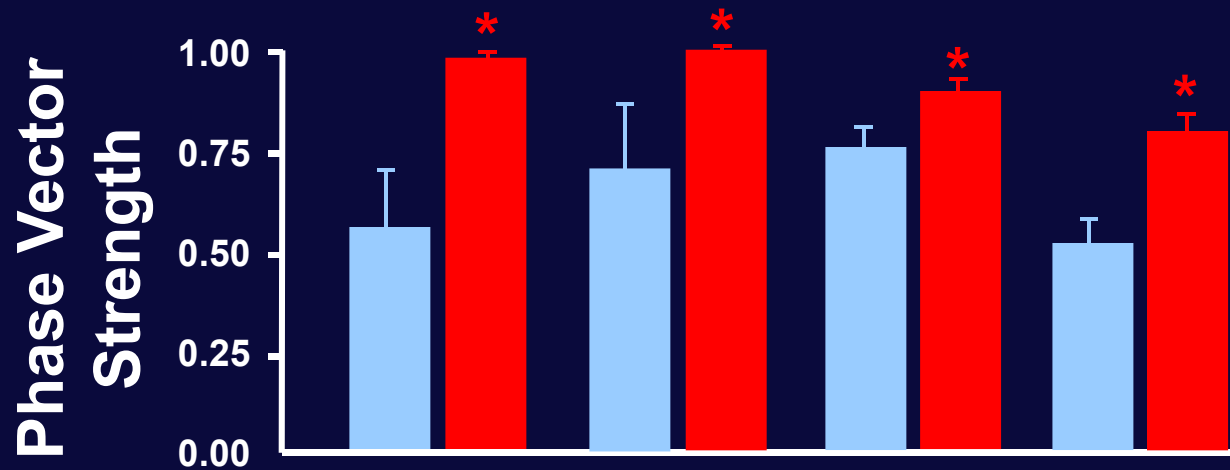
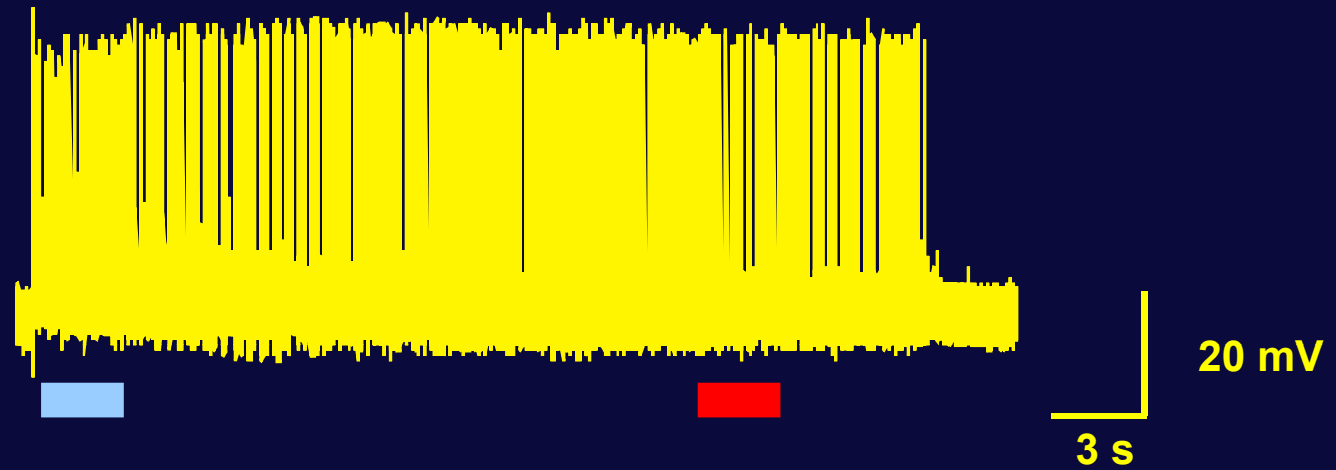
600 Hz



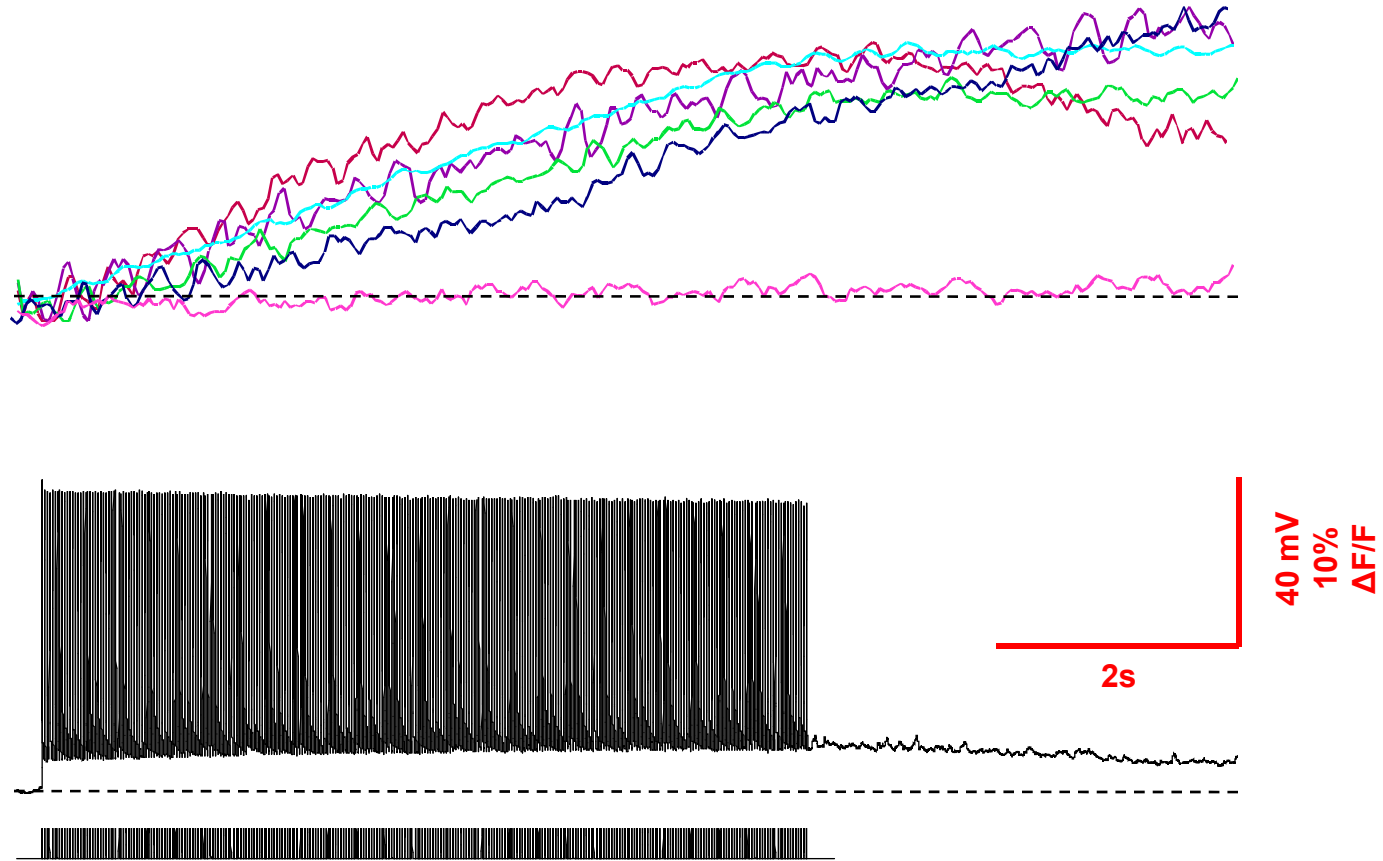
50 mV

25 ms

Temporal accuracy increases during high frequency stimulation



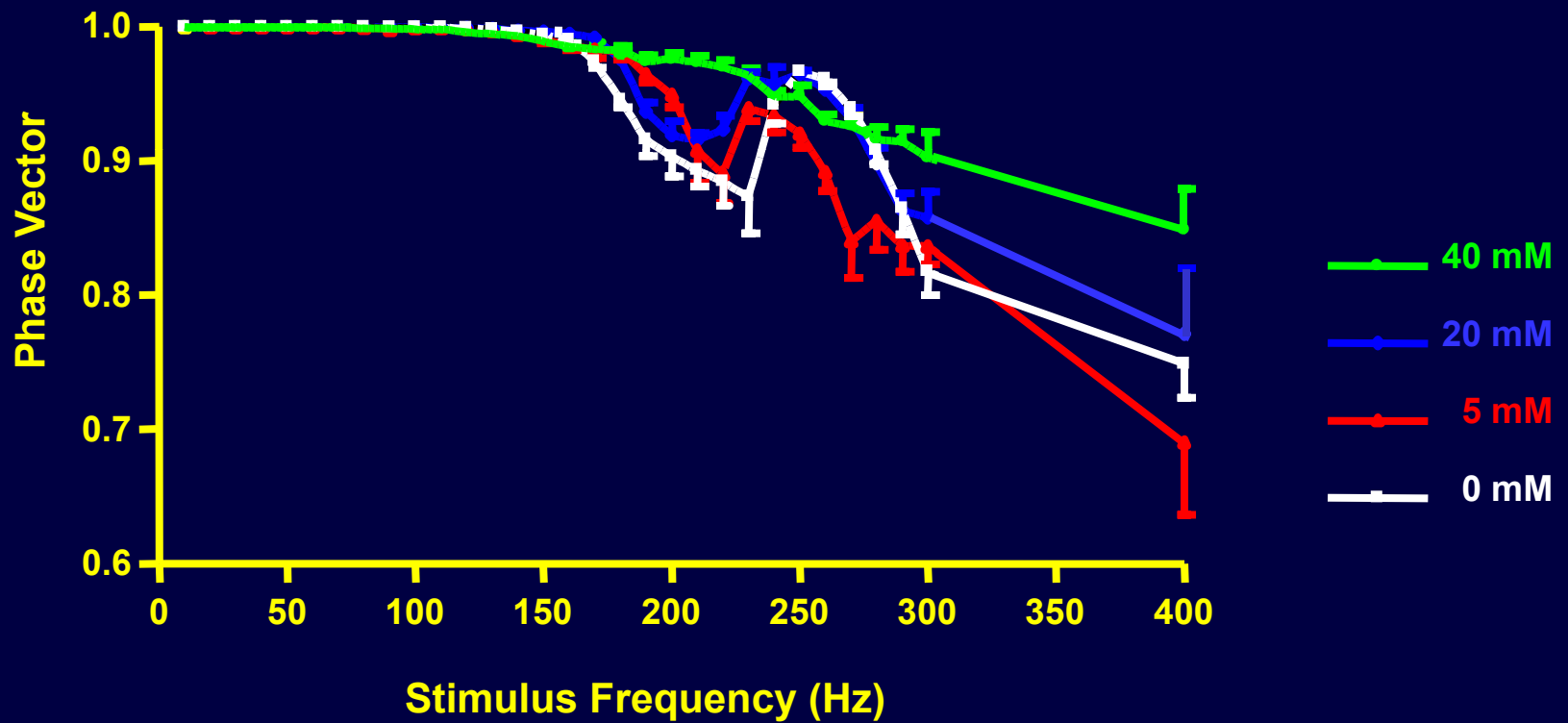
Na⁺ rises slowly during repetitive stimulation of auditory neurons



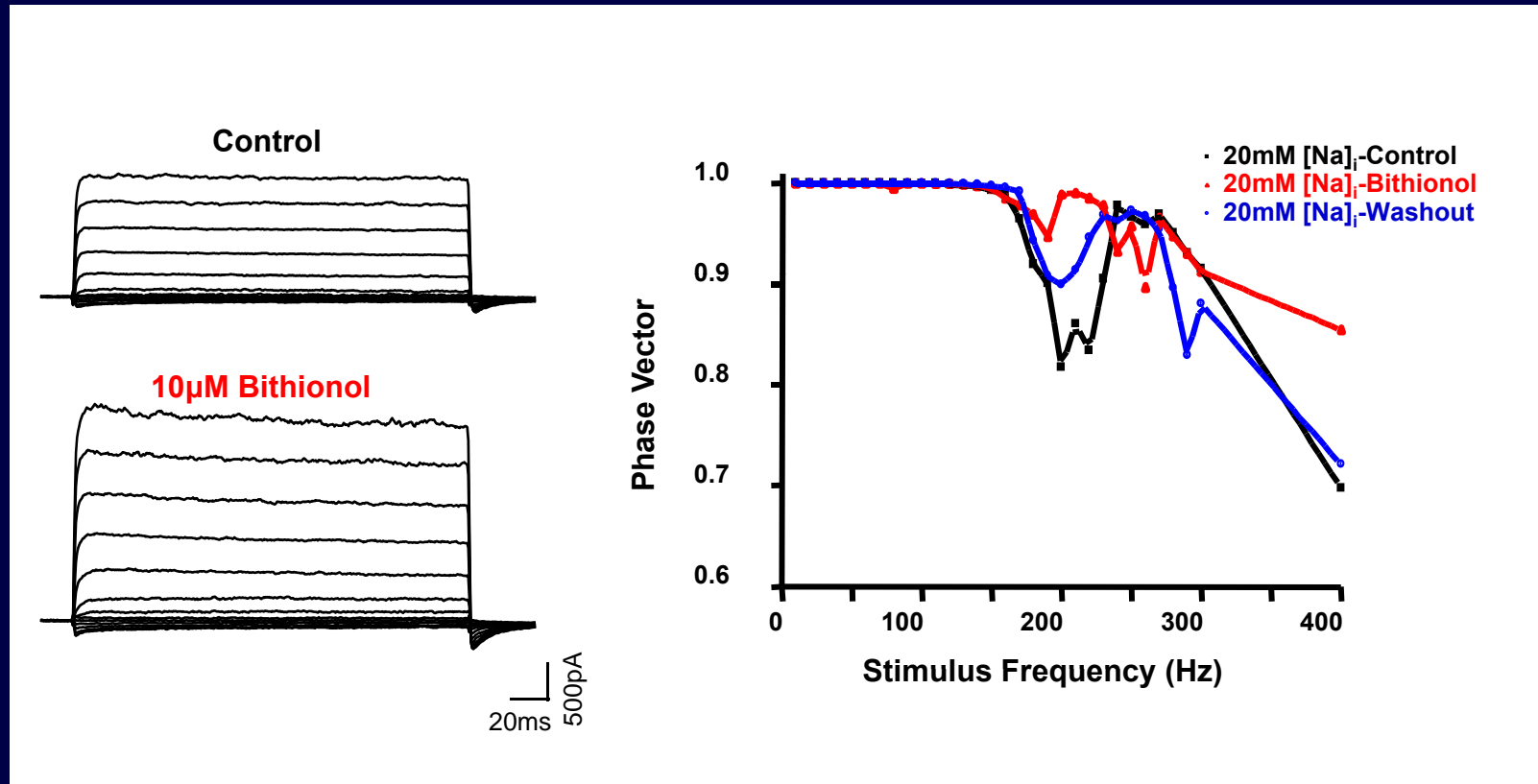
Intracellular Stimulus Train
(2 nA, 0.3 ms pulses at 50 Hz)

(bis-SBFI imaging)

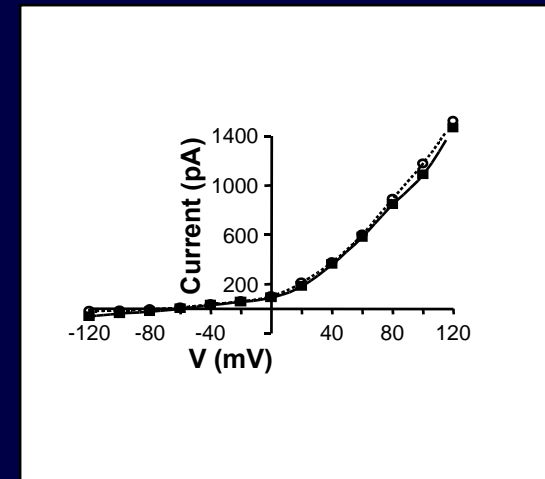
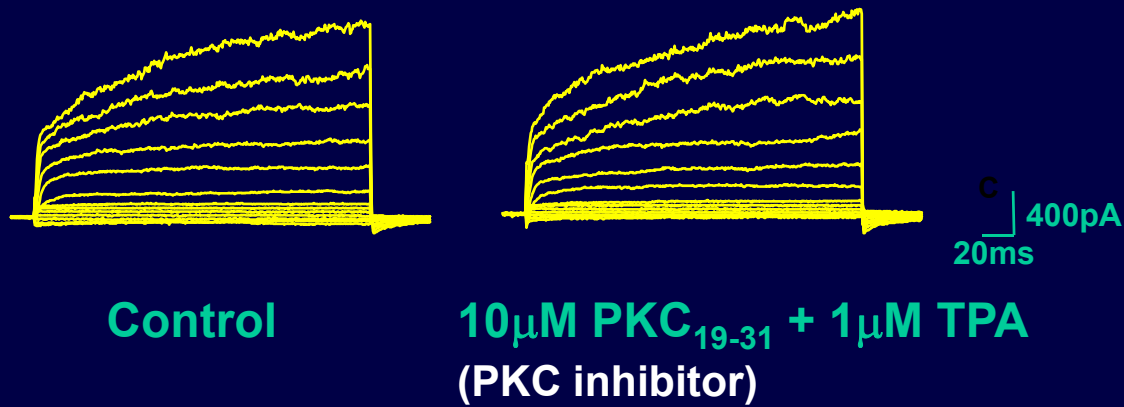
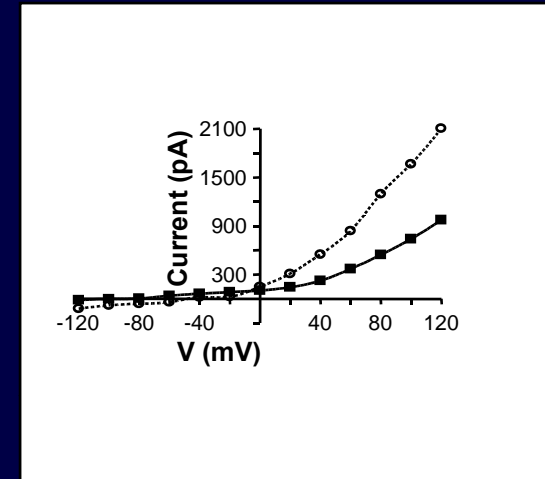
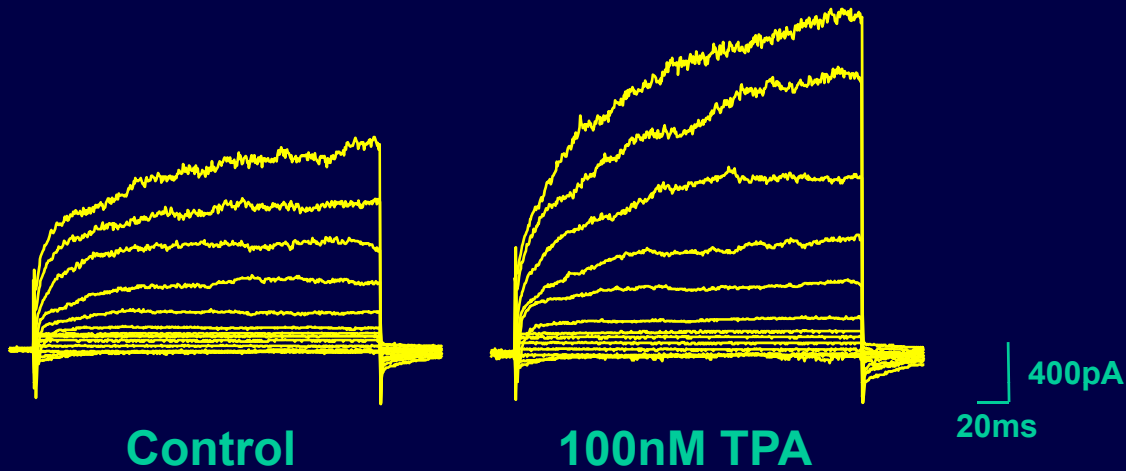
Elevated intracellular Na⁺ improves phase-locking in MNTB neurons



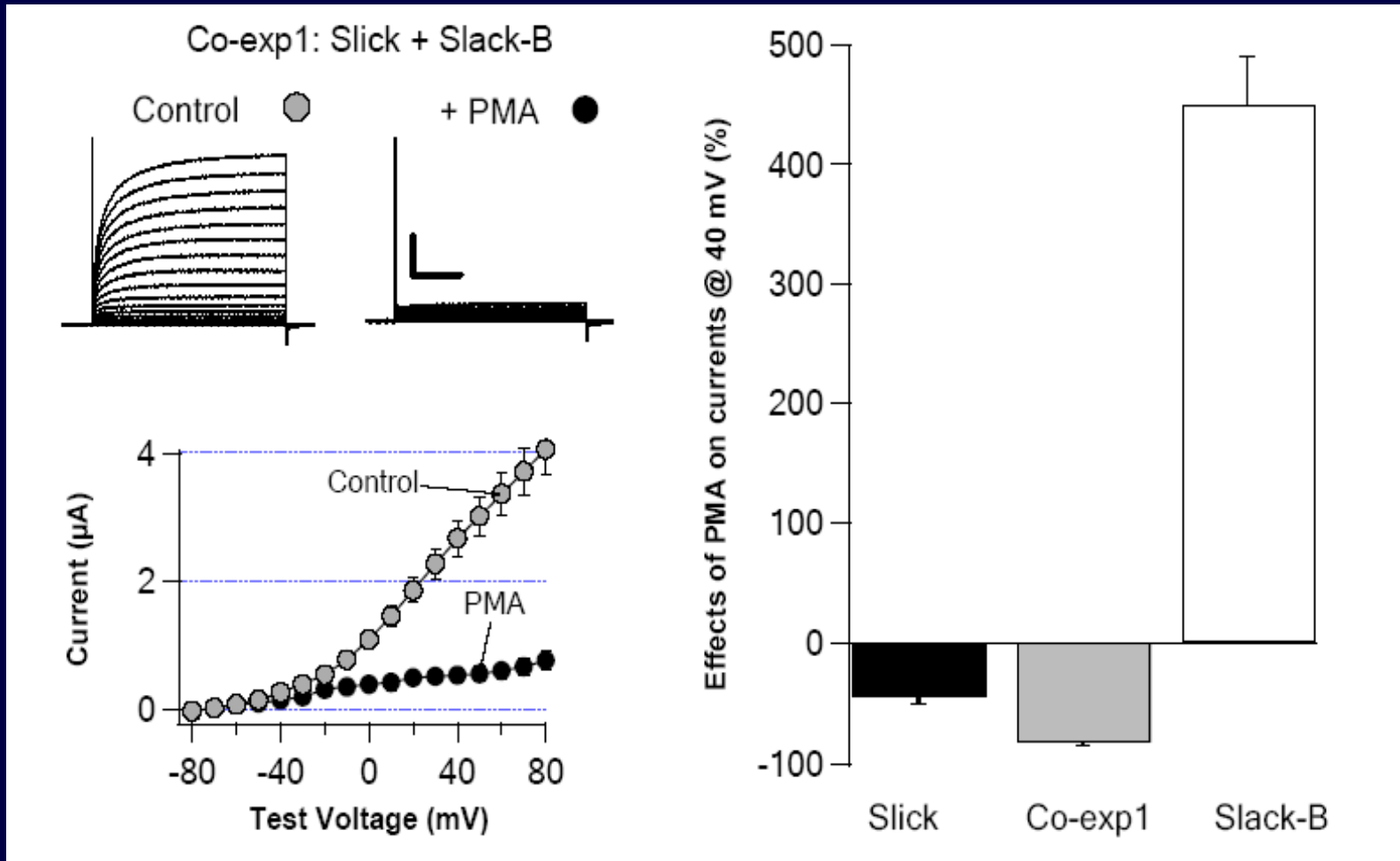
The Slack activator bithionol increases timing accuracy



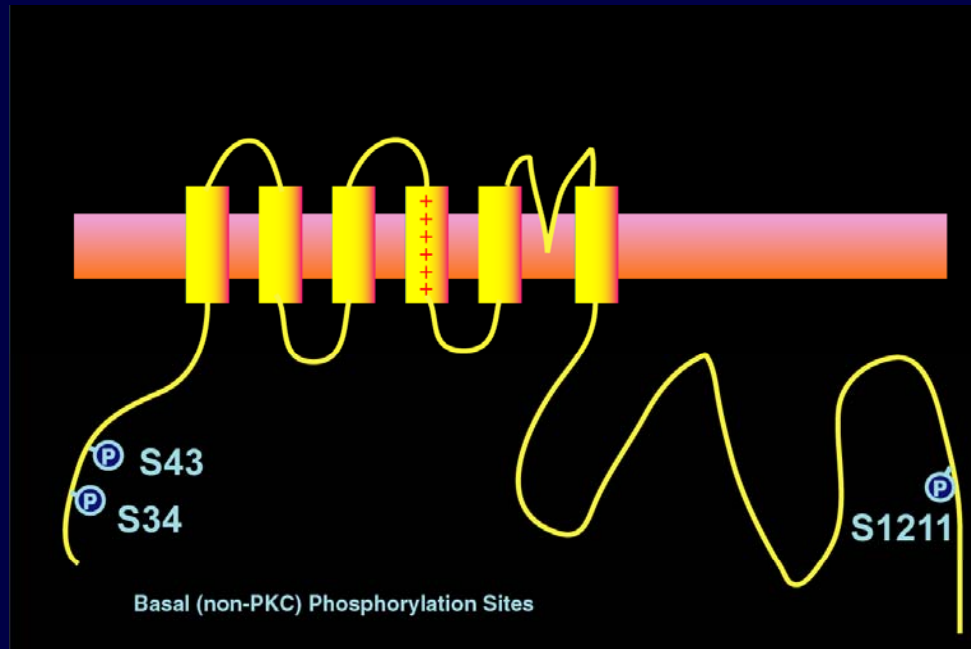
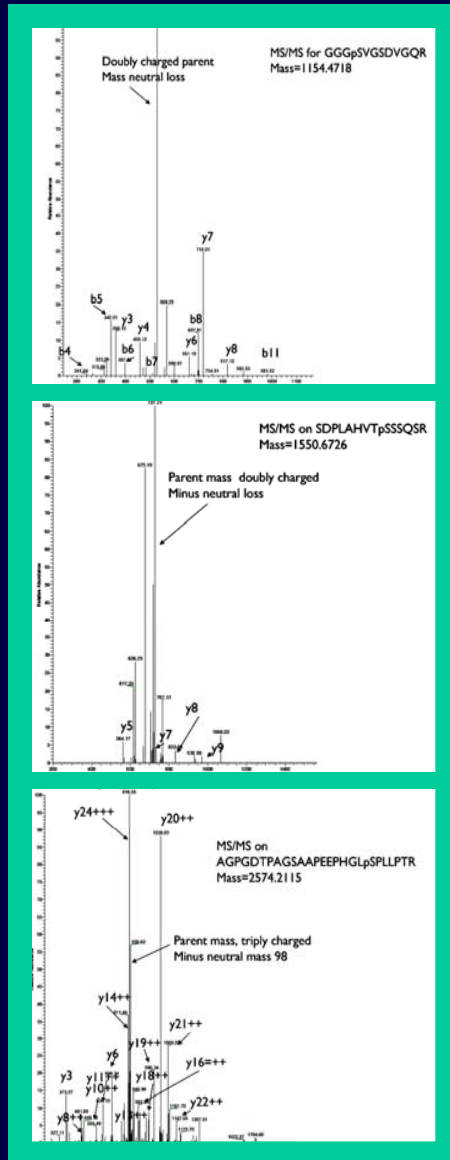
Activation of Protein Kinase C enhances Slack currents



Heteromeric Slack/Slick channels are strongly suppressed by PKC activation



Under basal conditions, Slack is phosphorylated on two N-terminal and one C-terminal serines



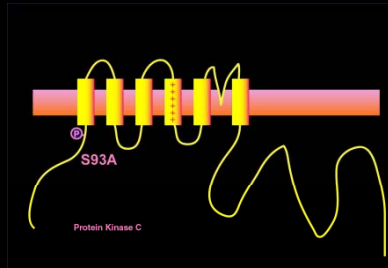
S34 **AGPGDTPAGSAAPEEPHGLpSPLLPTR**

S43 **GGGpSVGSDVGQR**

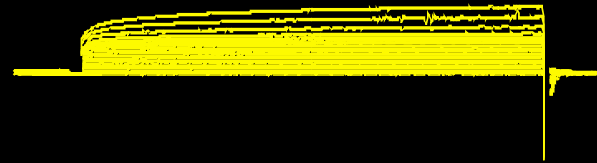
S1211 **SDPLAHTpSSSQRS**

Responses of Phosphorylation site mutants to PKC activation

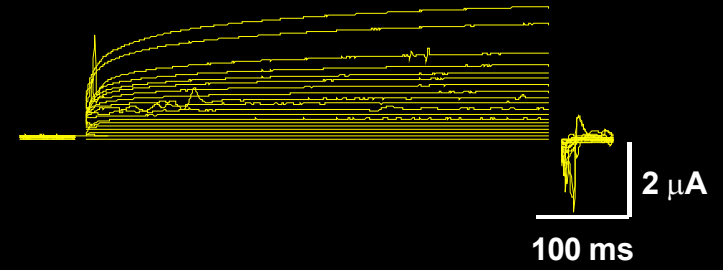
S39A



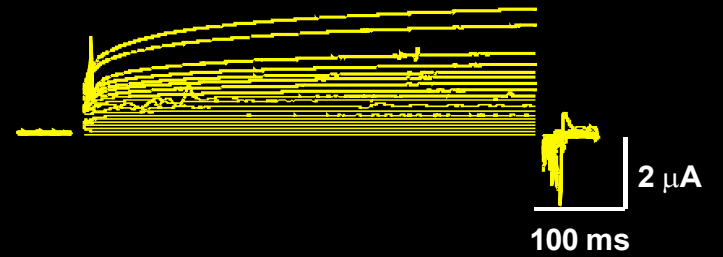
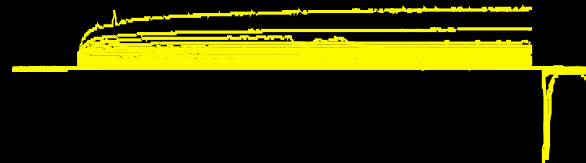
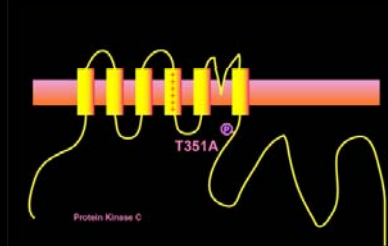
Control



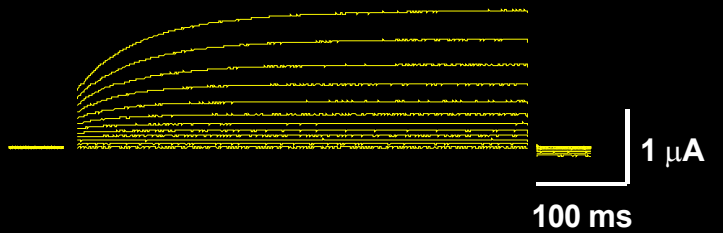
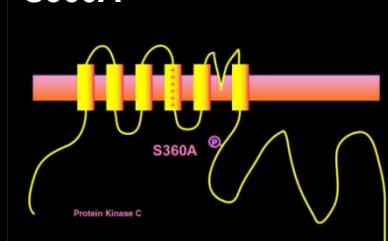
TPA



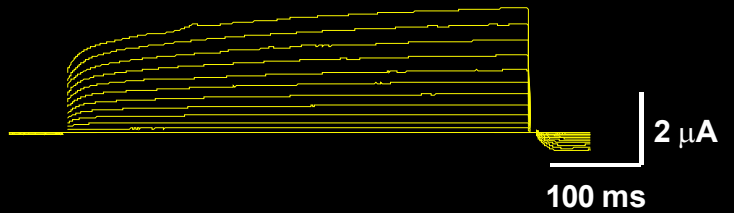
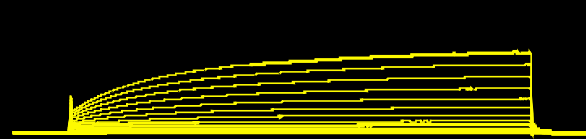
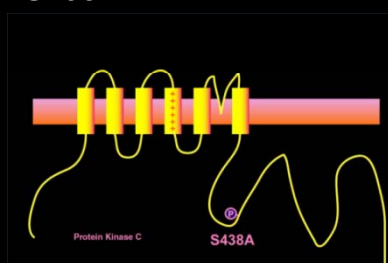
T351A



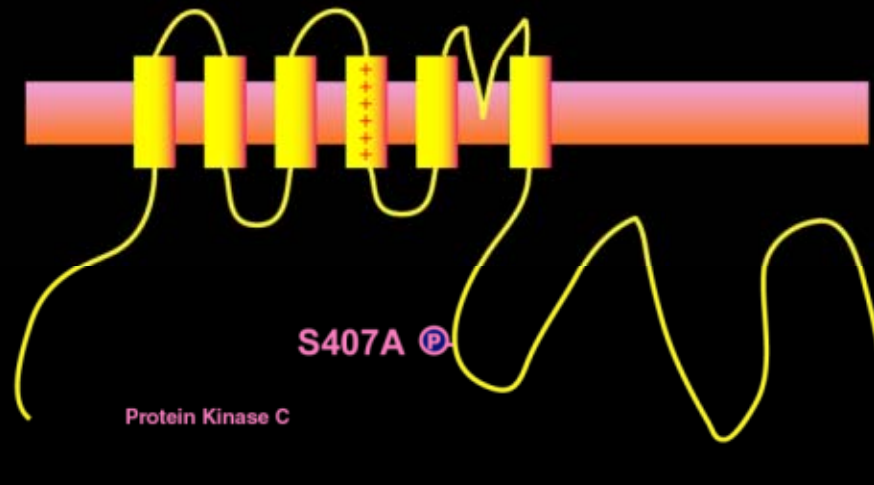
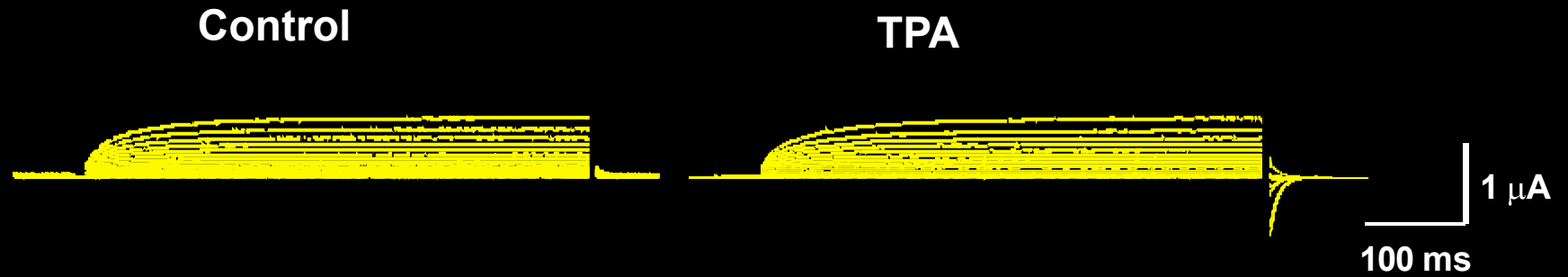
S360A



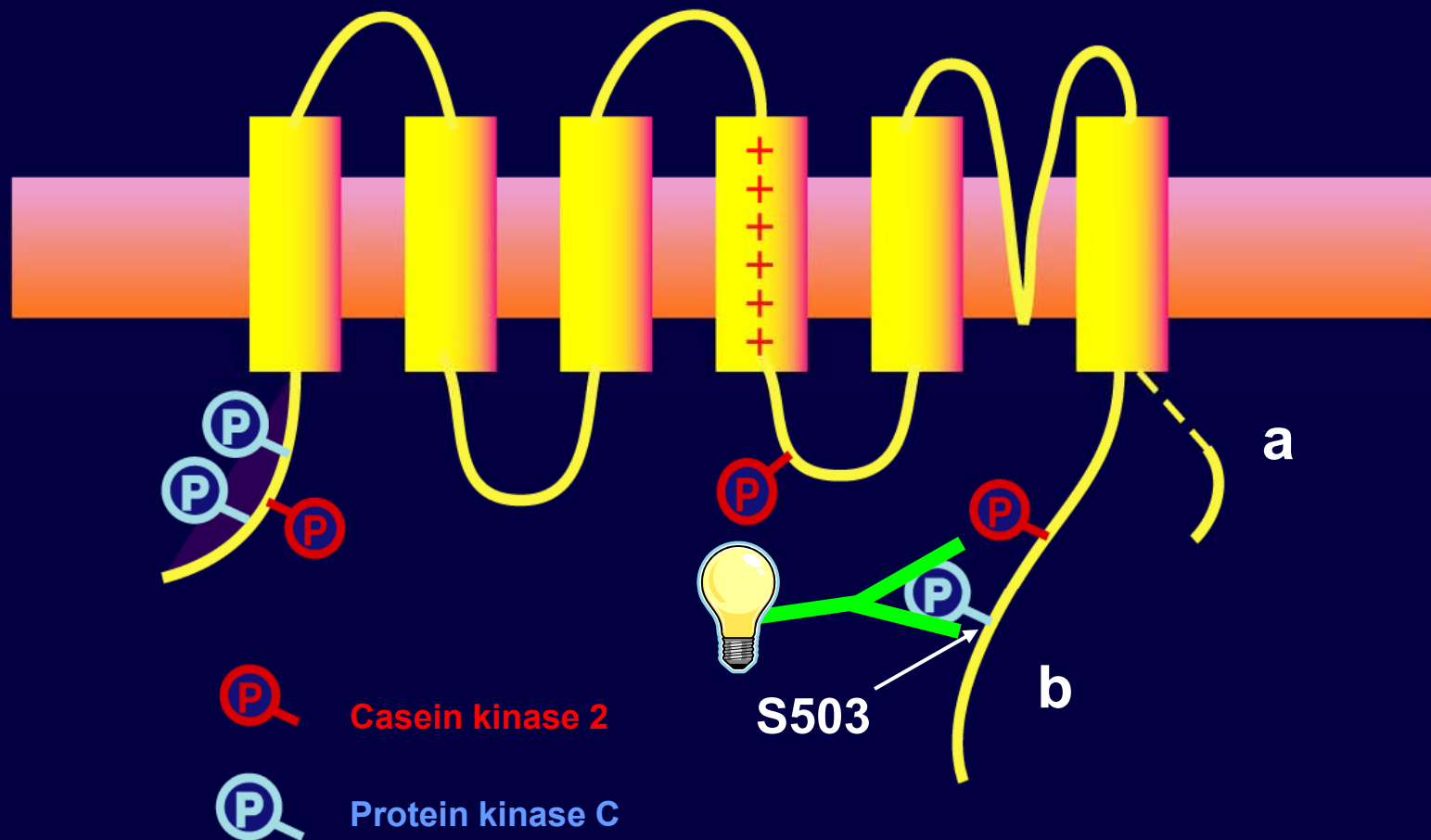
S438A



Slack mutant S407A fails to respond to PKC activation



Kv3.1



Effect of acoustic stimulation on Kv3.1 phosphorylation

MNTB

AVCN

Left

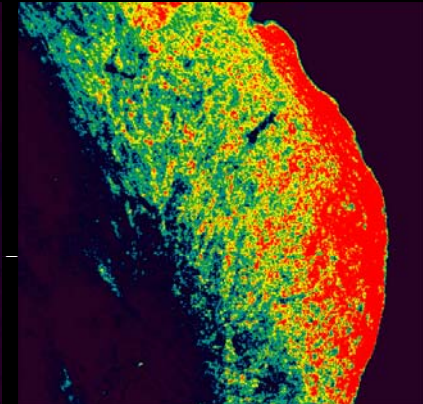
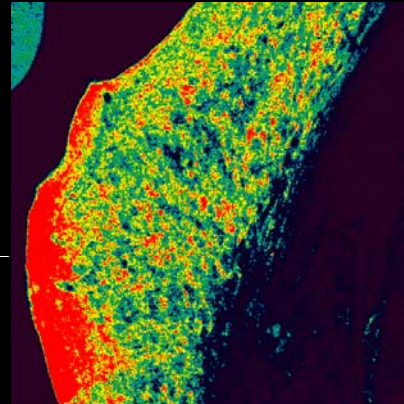
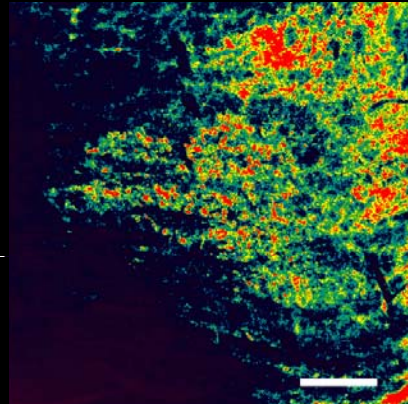
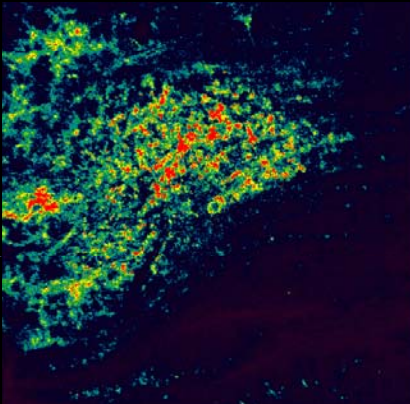
Control

Right

Left

Control

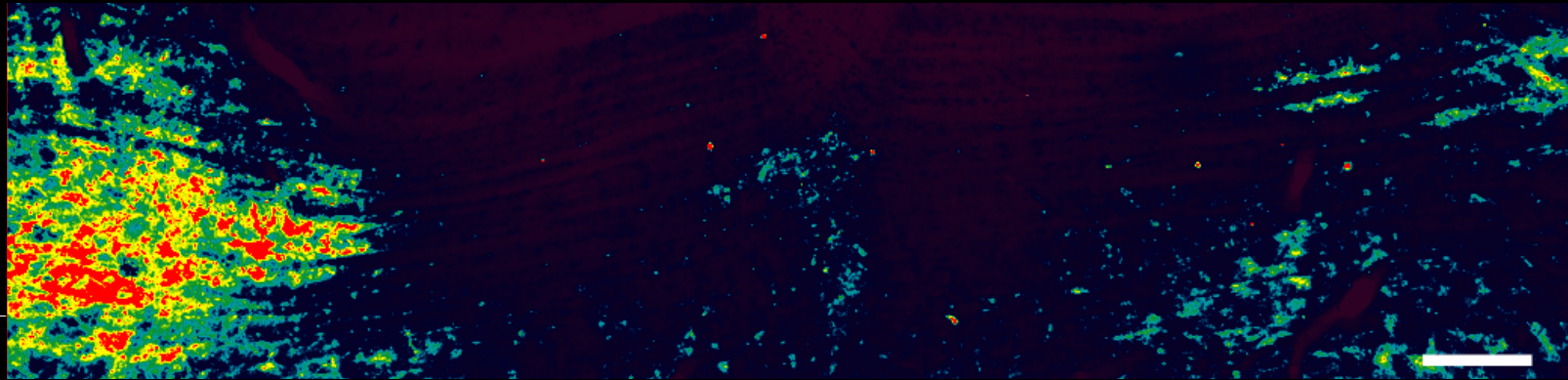
Right



Phosphorylation of Kv 3.1b in MNTB Neurons in vivo is decreased by acoustic stimulation

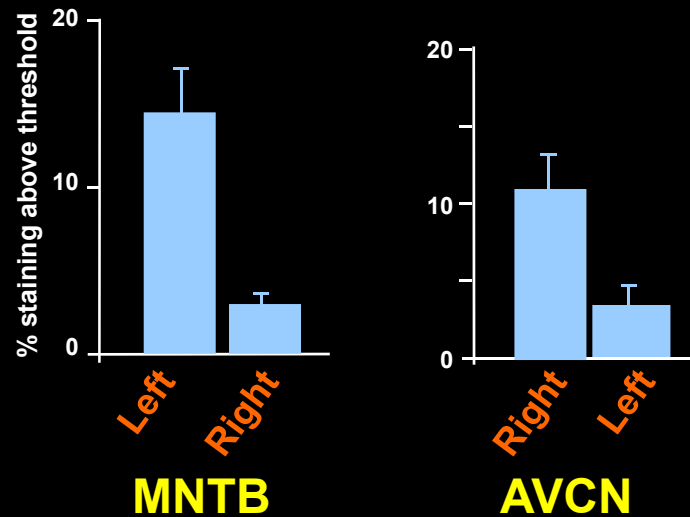
Left

Right

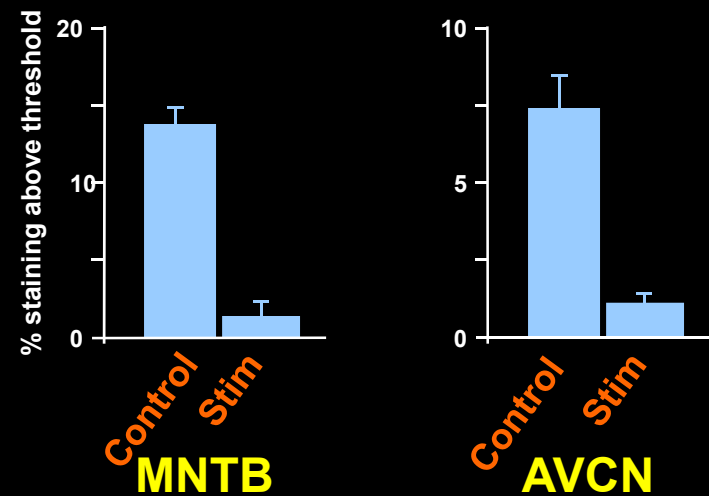


Monaural stimulation (click trains 600 Hz, 70 dB, 5 min) in left ear

Monaural stimulation (left ear)



Binaural stimulation



Matt Fleming

Haijun Chen

Bo Yang

Ping Song

Angus Nairn

TuKiet Lam

