Using axonal measurements of calcium to explore the role of parallel fiber excitation by $GABA_A$ receptors in a circuit dedicated to precise timing.

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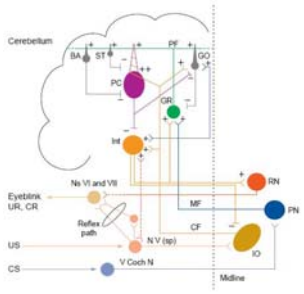
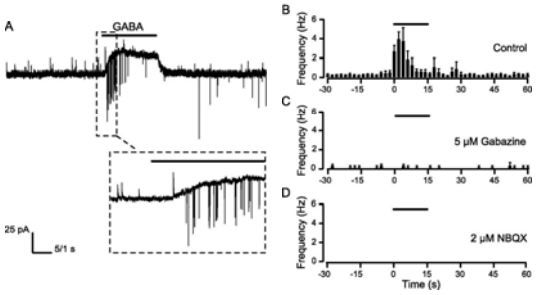
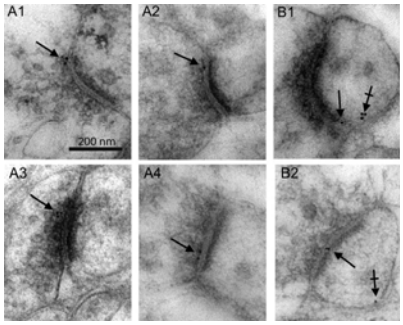
Parallel fiber (granule cell axons) innervate Purkinje cells and ML interneurons.



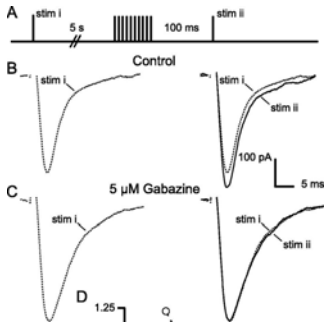

EPSCs in ML interneurons induced by $GABA_A$ activation (Stell et al, 2007).



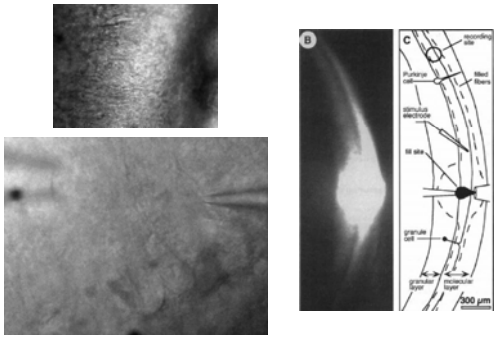

$GABA_AR\alpha_1$ subunits localized presynaptically to parallel fibers.



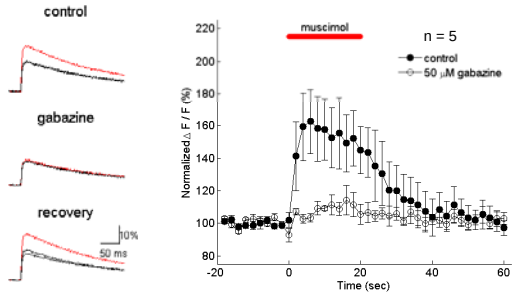

GABA released from interneurons by 100hz stimulation increases Purkinje cell EPSCs.



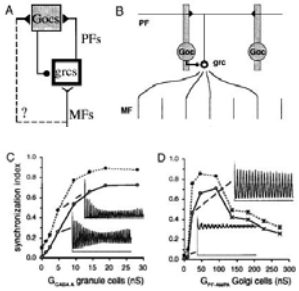

Local perfusion of calcium indicator limited to molecular layer and parallel fibers.



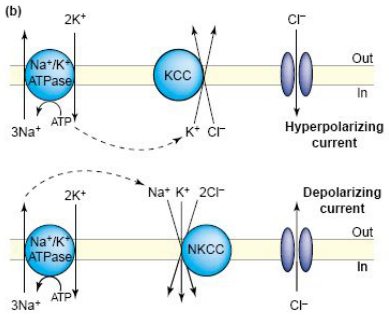
Presynaptic parallel fiber calcium transients are enhanced by $GABA_AR$ activation.



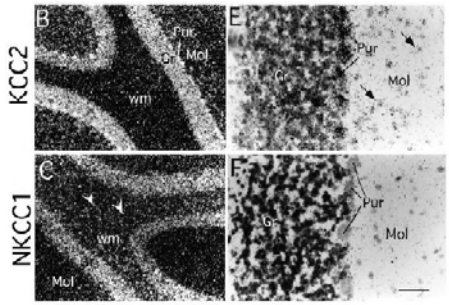

Predicted enhancement of feeback inhibition of granule cells (Maex et al, 1998).



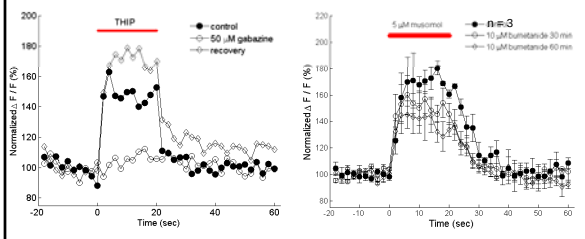

NKCC1 transporter is expressed early in development, and elevates internal $Cl^-$.




Cerebellar granule cells express mRNA of KCC, NKCC1 transporters (Mikawa, 2002).




Mechanism of GABA-mediated excitation of parallel fibers ($Cl^-$ gradient).



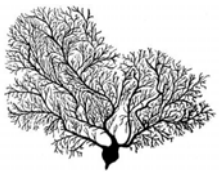

Future experiments.

- More physiological evoked enhancement.
- Uncage GABA in the molecular layer.
- Chloride indicator (MEQ, Clomeleon).
- Using TEA or high external K to increase signal.

In the Tom Otis lab, we do lots of experiments then sit there and think.

- Activation of $GABA_A$Rs leads to excitation of parallel fibers of the molecular layer.
- Excitation may help synchronize granule layer activity or enhance contrast in the system.
- Persistence of NKCC1 chloride transporters may provide a mechanism for GABAergic excitation.

In the Tom Otis lab, we study lots of cool stuff you can write home to mom about.



- Making it all possible:
  - Tom Otis.
- Big thank-yous:
  - Meera Pratap, Patty Araj.
  - Shlomo Dellal, Ka Hung Lee.
  - Paul Dodson (Edinburgh).
  - Movses Karakossian (Allergan, Irvine).
  - Sal Stella (Brecha lab).
  - Felix Schweizer lab.

Stell et al, 2007.

- 50uM GABA -> slow outward fast inward MLI.
- 2uM NBQX blocked fast inward -> glu release.
- Double exponential fit to events -> bursts.
- CV w/i bursts > CV of sEPSCs -> single fiber.
- Fatigue of effect to 10 min -> Cl concentration.
- Not diffusion of muscimol to granule layer b/c moving away from ML attenuates response.
- 20mM K -> no change sEPSC freq -> not MLI K.