Effect of various recoding of granule cells on Pavlovian eyeblink conditioning in a cerebellar network

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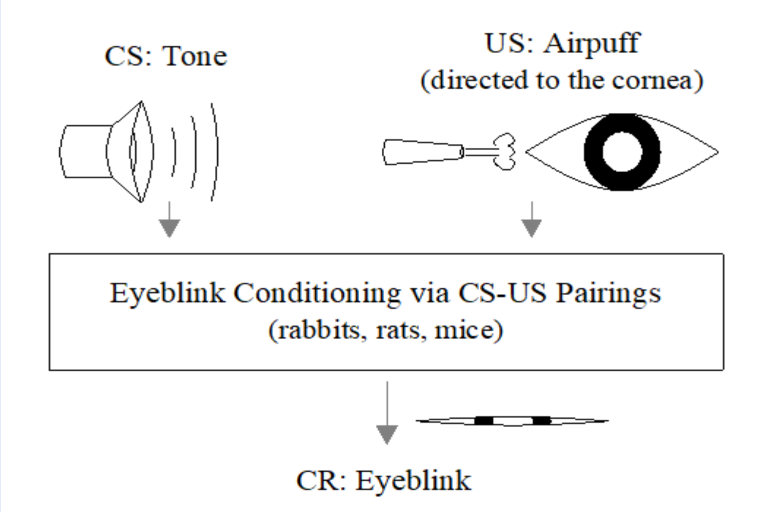
- **Cerebellar Motor Learning**
  - Precise temporal and spatial motor control for coordinating voluntary movements (e.g. posture, balance, and locomotion)
  - Timing: Temporal information of movements [e.g. initiation or termination]
  - Gain: Spatial information of movements



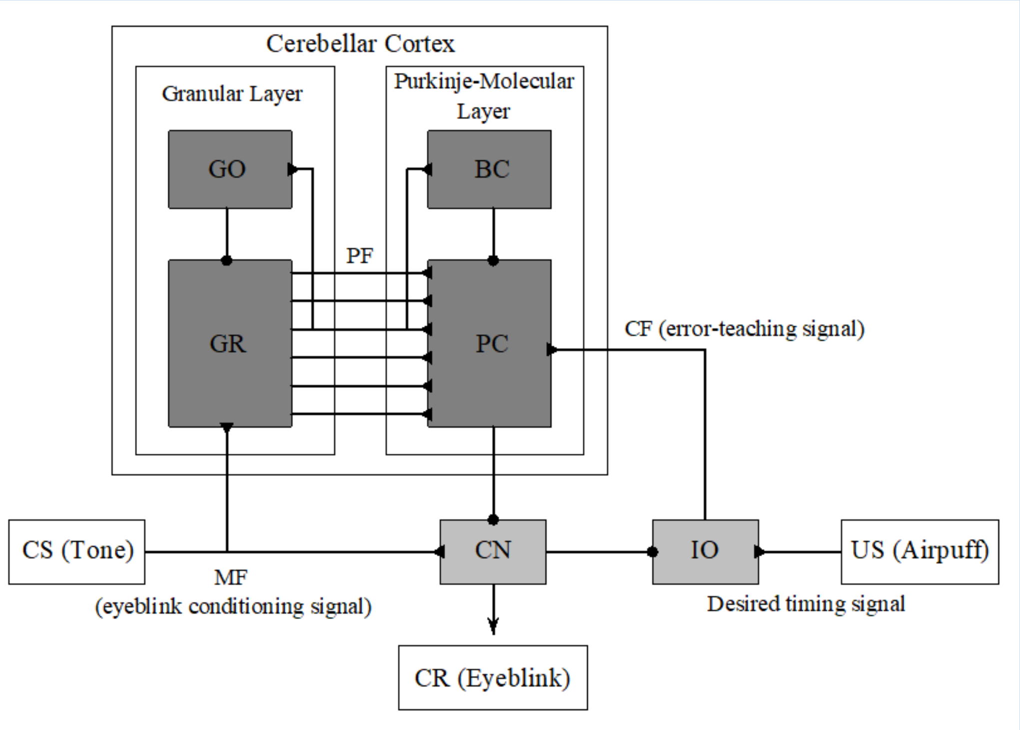
- **Pavlovian Eyeblink Conditioning (EBC)**
  - Repeated presentations of paired conditioned stimulus (CS; tone) and (eyeblink-eliciting) unconditioned stimulus (US; airpuff).
  - Eyelid conditioned response (CR) via learning representation of the time passage between the onsets of CS and US

- **Purpose of Our Study**

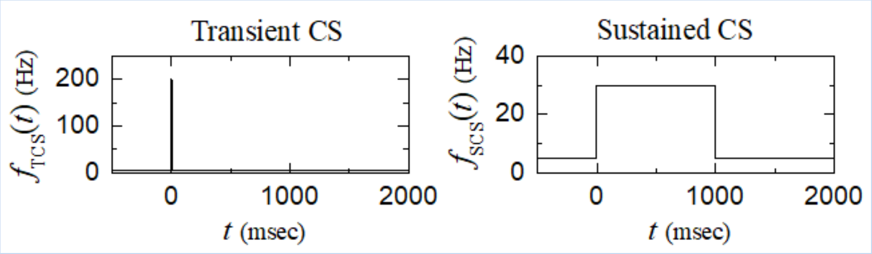
  Investigation of Effect of Various Recoding of Granule Cells on Pavlovian EBC in A Cerebellar Ring Network by Varying The Connection Probability p_c from The Golgi Cells to The Granule Cells

Cerebellar Network for EBC

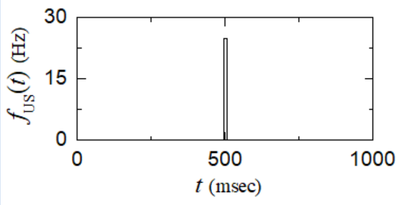
- **Cerebellar Network for Pavlovian EBC**
  - Granular Layer: Input layer of cerebellar cortex
    Excitatory granule (GR) cells
    & Inhibitory Golgi (GO) cells
  - Purkinje-Molecular Layer:
    Output Layer
    Inhibitory Purkinje cells (PCs)
    & basket cells (BCs)



  - Context signal for the EBC via mossy fiber (MF): Transient Conditioned Stimulus (CS) for resetting and sustained CS (representing the tone)

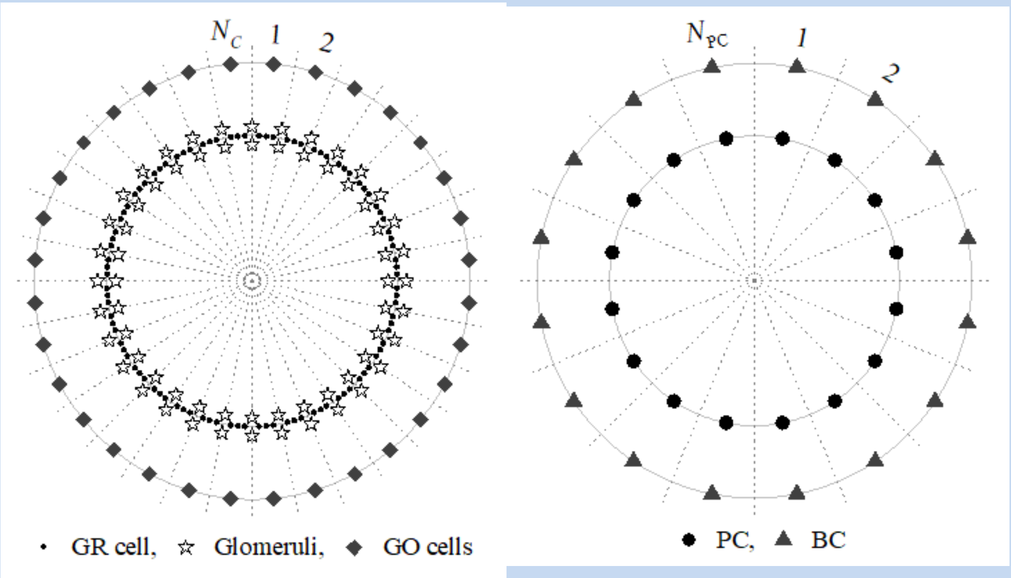


  - Desired timing signal Unconditioned Stimulus (US) into inferior olive (IO)



Cerebellar Ring Network & Synaptic Plasticity Rule

- **Cerebellar Ring Networks**
  - Granular-Layer Ring Network
    $N_C (= 2^{10})$ GR clusters
    $N_{\mathrm{GR}} (= 50)$ GR cells in each GR cluster
    N_C GO cells
    Each GR cluster bounded by four glomeruli (GL): Upper & lower GLs
    Each GL: One MF & ~ 2 GO cells
    $(p_c = 0.029)$
  - Purkinje-Molecular-Layer Ring Network
    $N_{PC} (= 16)$ PCs and basket cells (BCs)



- **Refined Rule for Synaptic Plasticity**

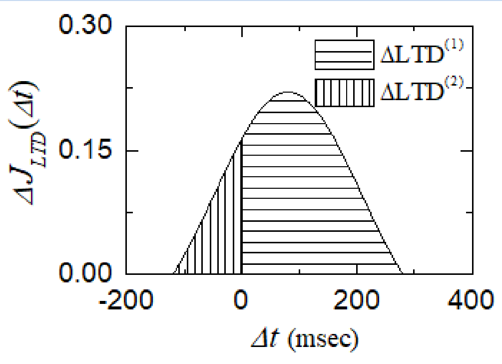
$$J_{ij}^{(\mathrm{PC,PF})}(t) \rightarrow J_{ij}^{(\mathrm{PC,PF})}(t) + \Delta\mathrm{LTD}_{ij}^{(1)} + \Delta LTD_{ij}^{(2)} + \Delta\mathrm{LTP}_{ij}$$

- Synaptic modification (LTD or LTP) depending on the relative time difference between CF & PF activation times

$\Delta\mathrm{LTD}_{ij}^{(1)}$: Major LTD in the case that the CF signal is associated with earlier PF signals

$\Delta LTD_{ij}^{(2)}$: Minor LTD in the case that the CF signal is related to later PF signals

$\Delta\mathrm{LTP}_{ij}$: LTP in the presence of PF signals alone without association with the CF signal

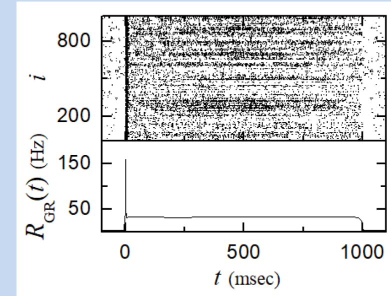


$$\Delta J_{LTD}(\Delta t) = A + B \cdot e^{-[(\Delta t - t_0)/\sigma]^2}$$

$$A = -0.12,\ B = 0.4,\ t_0 = 80,\ \sigma = 180$$

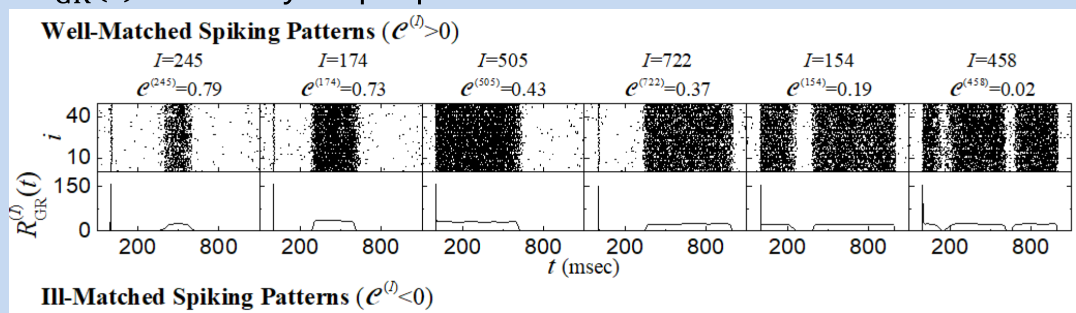
Various Firing Patterns in The GR Clusters

Optimal case: $p_c^* = 0.029$



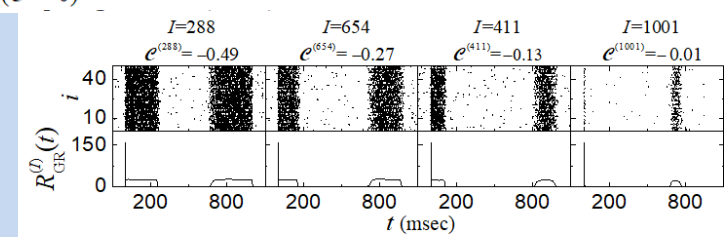
• Firing Activity in The Whole GR Cells

- Raster plot of spikes of 10^3 randomly chosen GR cells:
  Beginning of trial stage: all GR cells fire due to strong transient CS signal
  Remaining part of the trial stage: GR cells make random repetition of transitions between active and inactive states because of sustained CS signal
- Instantaneous whole-population spike rate $R_{GR}(t)$: Basically in proportion to the transient and sustained CS inputs via MFs
- Due to the inhibitory effect of GO cells, the overall firing rates: Uniformly lowered



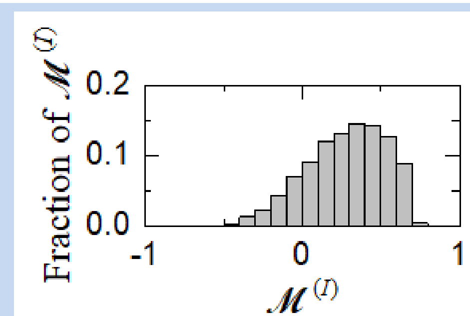
• Various Firing Patterns in GR clusters

- $R_{GR}^{(I)}(t)$: Instantaneous cluster spike rate in the Ith GR cluster
- Various firing patterns $R_{GR}^{(I)}(t)$: Well- & ill-matched with respect to US [$f_{US}(t)$]



• Characterization of Various Firing Patterns

- Matching index $\mathcal{M}^{(I)}$: Cross-correlation
  between $R_{GR}^{(I)}(t)$ and $f_{US}(t)$ at the zero-time lag
  Well-matched firing group → $\mathcal{M}^{(I)}>0$
  Ill-matched firing group → $\mathcal{M}^{(I)}<0$
- Variety Degree $\mathcal{V}$: Relative standard deviation of $\{\mathcal{M}^{(I)}\}$ $\mathcal{V}$=1.842

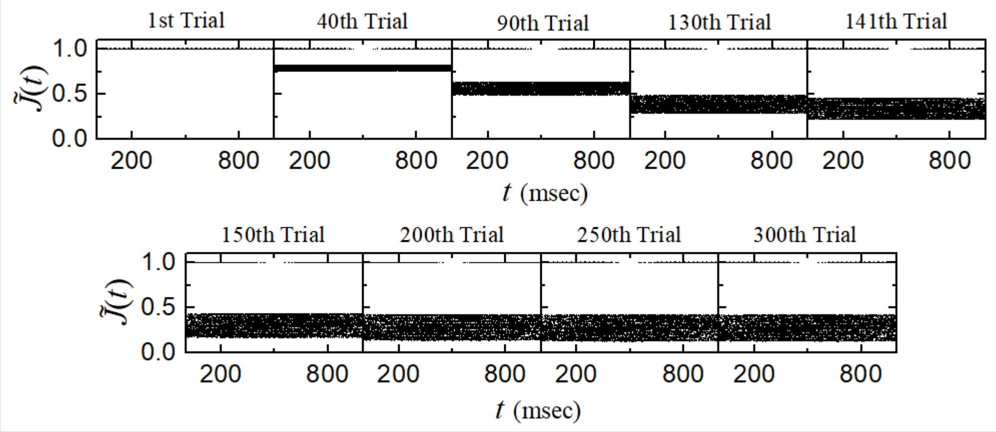


Change in PF-PC Synaptic Weights during Learning

- **Distribution of Normalized Active PF-PC Synapses**
  - Combination of separate top horizontal line with a central gap and lower band
  - Horizontal line: No essential change with trials

    Arising from ill-matched firing group with a central gap

    No LTD because of no associations with error-teaching CF signal

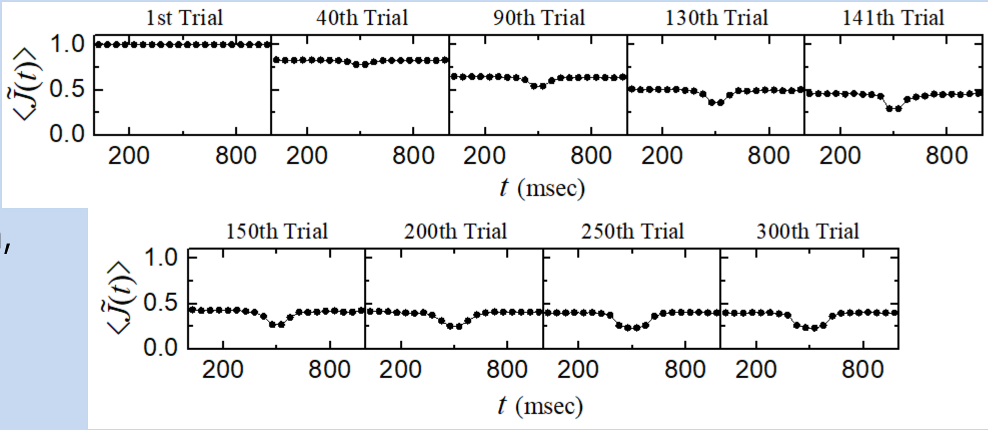


  - Lower band: Increase in vertical width & Saturated at about the 250th trial

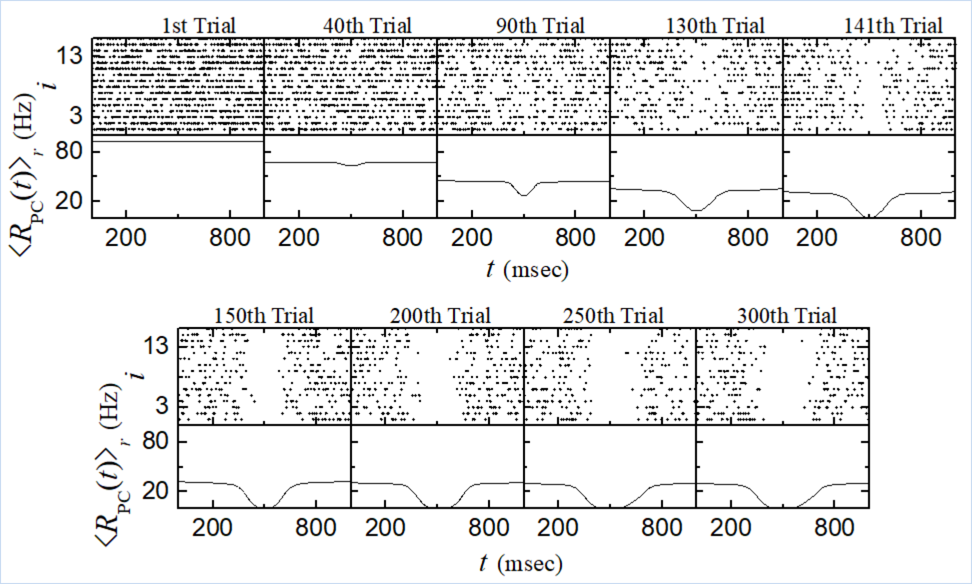
    Arising from well-matched firing group

    Strong LTD due to good association between the well-matched PF and CF signals

- **Bin-averaged Synaptic Weights $\langle \tilde{J} \rangle$ of Active PF**
  - Step-well-shaped curve
  - With the trial, step-well curve comes down, increase in its width & depth, and saturation at about the 250th trial



Change in Firing Activity of PCs during Learning



- **Raster Plots of Spikes**

  Increase in trial, more sparse at the middle part due to strong LTD

- **Population Spike Rates $\langle R_{PC}(t)\rangle_r$ of PCs**

  - Step-well-shaped curve
  - With the trial, the step-well in the middle part comes down, a zero-bottom appears in the middle part at the 141th trial

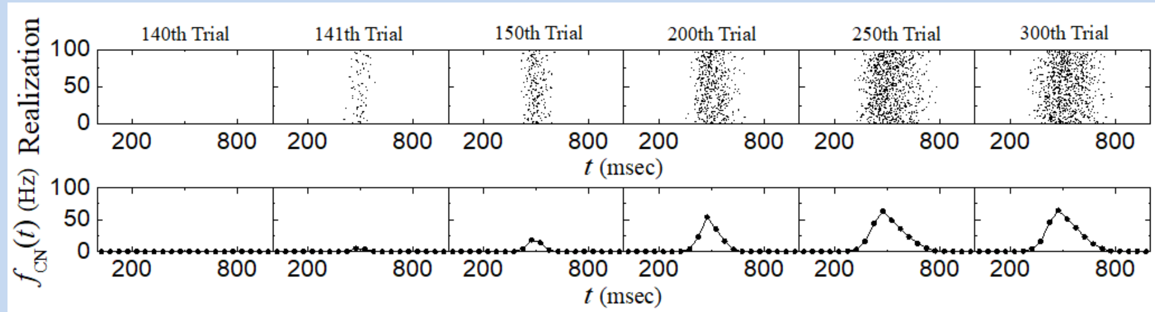
    → CN (cerebellar nucleus) neuron which evokes CR (conditioned response: eyeblink)

    CN neuron fire spikes
  - With increase in the trial from the 141th trial, increase in the (top) width of the step well and the width of the zero-bottom.

Change in Firing Activity of CN during Learning

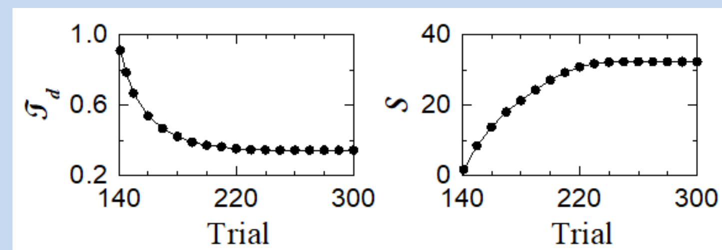
• Firing Activity of CN during Learning

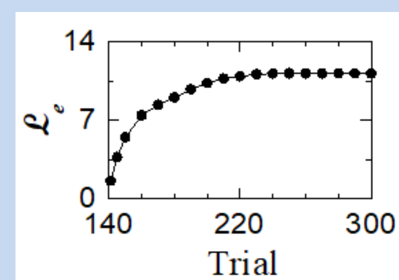
- 140th trial: No firing due to strong inhibition from PC
- CN neuron begins to fire in the middle part at the 141th trial due to appearance of a zero-bottom in PC
- With increasing the trial, raster plots of spikes of the CN neuron become more dense in the middle part
- Instantaneous individual firing rates $f_{\rm CN}(t)$: Bell-shaped curve.
  With the trial, increase in bottom-base width and peak height, and saturated at about the 250th trial



• Learning Efficiency Degree

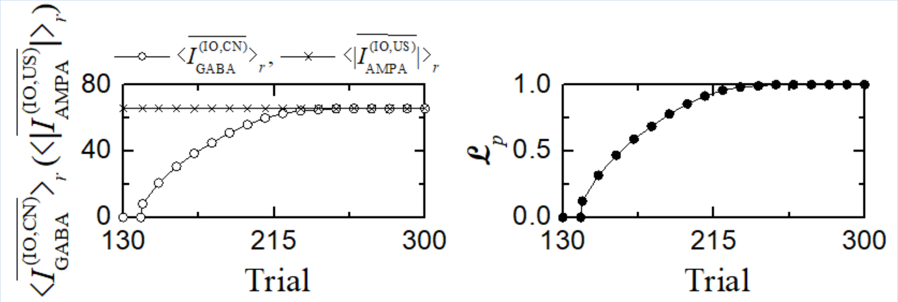
- Timing degree $\mathcal{T}_d$: Matching degree between the firing activity of CN and US signal
  Cross-correlation between $f_{\rm CN}(t)$ & $f_{\rm US}(t)$ at the zero-time lag: Reflecting width of the bottom base of the bell curve
  With the trial, decrease in $\mathcal{T}_d$, and saturated at about the 250th trial
- Strength $\mathcal{S}$ of CR: Representing the amplitude of the eyelid closure
  Modulation [(maximum – minimum)/2] of $f_{\rm CN}(t)$
  With the trial, increase in $\mathcal{S}$, and saturated at about the 250th trial
- Learning efficiency degree $\mathcal{L}_e$ for CR: $\mathcal{L}_e = \mathcal{T}_d \cdot \mathcal{S}$
  With the trial, increase in $\mathcal{L}_e$, and saturated at about the 250th trial





Learning Progress in The IO System

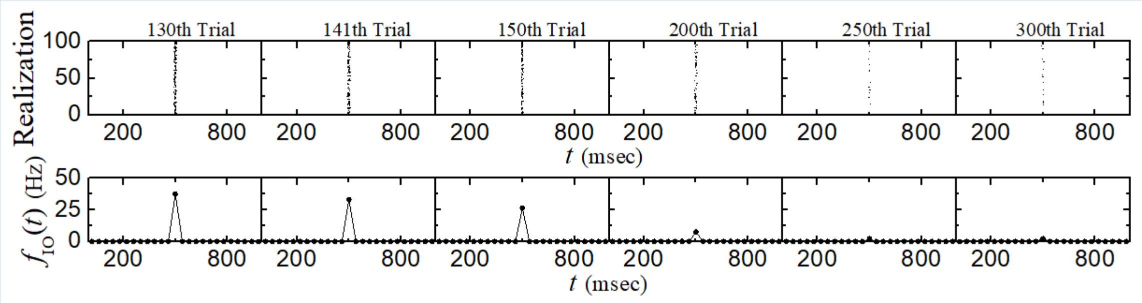
- **Learning Progress**
  - Two inputs into IO: Excitatory US signal for the desired timing and the inhibitory signal from CN (representing a realized eye-movement)



  - After acquisition of CR, with increasing trial, increase in inhibitory input from the CN, and convergence to the constant excitatory input through the US signal.
  - Learning progress degree $\mathcal{L}_p = \overline{I_{\text{GABA}}^{(\text{IO,CN})}} / \overline{\left| I_{\text{AMPA}}^{(\text{IO,US})} \right|}$

    With the trial, increase in $\mathcal{L}_p$, and saturated at 1 at about the 250th cycle.

- **Firing Activity of IO neuron during Learning**
  - Before the 141th threshold trial, dense spikes appear in the middle part due to excitatory US signal.



  - With increasing the trial from the threshold, spikes become sparse, because of increased inhibitory input from the CN neuron, and saturated at abut the 250th trial

Summary

- **Various Temporal Recoding in The GR clusters**

  Appearance of various well- and ill-matched firing patterns, due to inhibitory coordination of GO cells

  Characterized in terms of matching index and variety degree

- **Effect of Various Recoding on The EBC**

  Effective depression at the PF-PC synapses

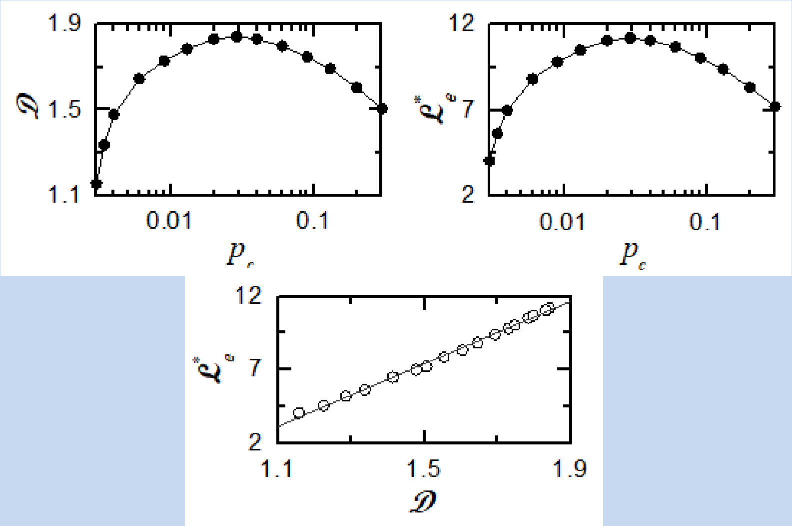
  Well-matched PF signals: Strong LTD by the CF signals, Ill-matched PF signals: Practically no LTD

  → Effective modulation in firing of PCs & CN Neuron

- **Relation between Various Recoding and Learning Efficiency Degree**

  - Strong Correlation between Variety Degree $\mathcal{D}$ and Saturated Learning Efficiency Degree $\mathcal{L}_e^*$

  Bell-shaped curves with maximum at the same optimal value of $p_c^* = 0.029$



The more various in temporal recoding of granule cells

→ The more effective in motor learning for the Pavlovian EBC