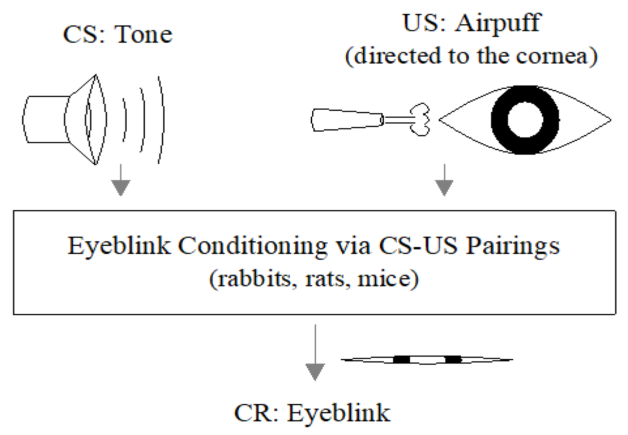
Effect of Diverse Recoding of Granule Cells on Delay Eyeblink Conditioning in A Cerebellar Network

Sang-Yoon Kim and Woochang Lim

Institute for Computational Neuroscience and Department of Science Education, Daegu National University of Education, Daegu 42411, S. Korea

Introduction

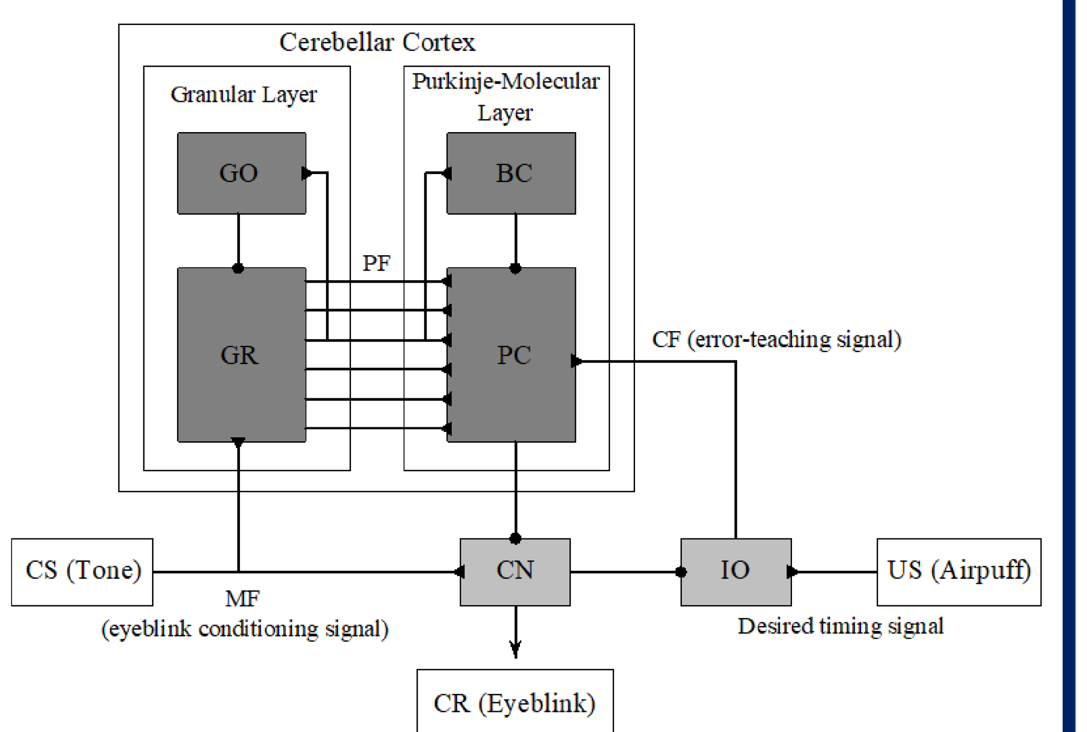
- **Cerebellar Motor Learning**
  - Precise temporal and spatial motor control for coordinating voluntary movements (e.g. posture, balance, and locomotion)
  - Timing: Temporal information of movements [e.g. initiation or termination]
  - Gain: Spatial information of movements
- **Pavlovian Eyeblink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

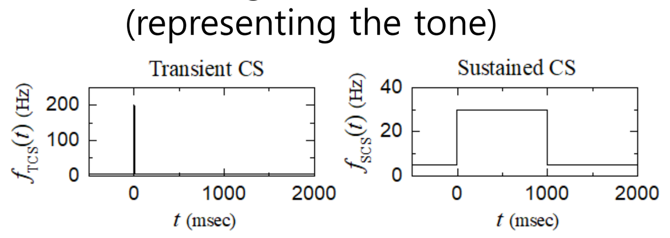


- **Purpose of Our Study**
  Investigation of Effect of Diverse Recoding of Granule Cells on Pavlovian EBC in A Cerebellar Ring Network by Varying The Connection Probability p_c from The Golgi Cells to The Granule Cells

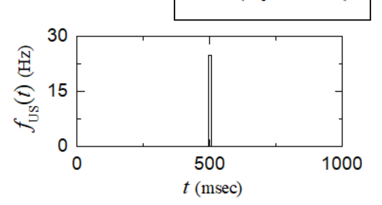
Cerebellar Ring Network for The EBC

- **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)

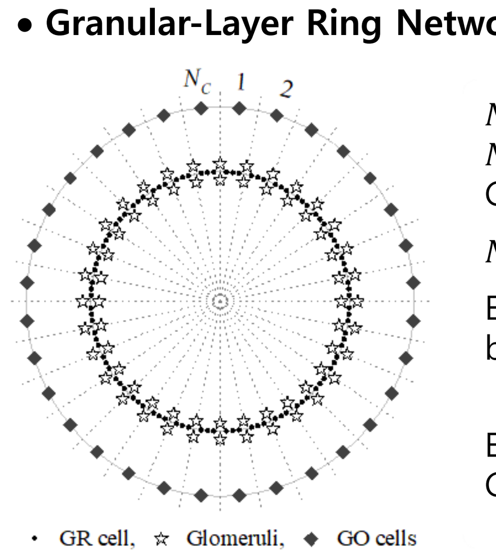




  - Desired timing signal Unconditioned Stimulus (US) into inferior olive (IO)



- **Granular-Layer Ring Network**



$N_C(=2^{10})$ GR clusters

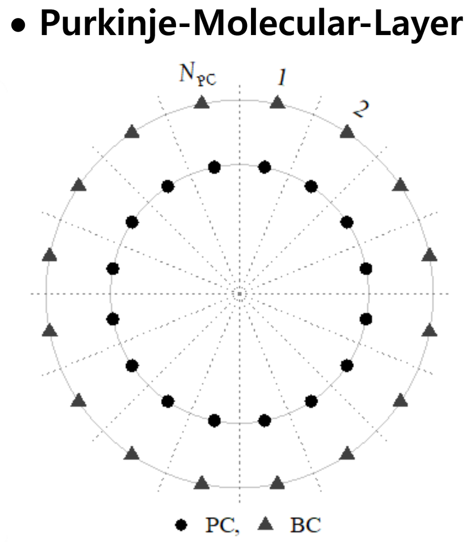
$N_{GR}(=50)$ GR cells in each GR cluster

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 & BCs

- **Refined Rule for Synaptic Plasticity at Parallel Fiber(PF)-PC Synapse**

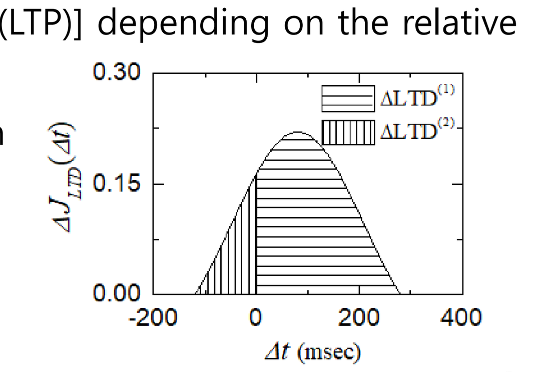
$$J_{ij}^{(\mathrm{PC,PF})}(t) \to J_{ij}^{(\mathrm{PC,PF})}(t) + \Delta\mathrm{LTD}_{ij}^{(1)} + \Delta\mathrm{LTD}_{ij}^{(2)} + \Delta\mathrm{LTP}_{ij}$$

  - Synaptic modification [long-term depression (LTD) or potentiation (LTP)] depending on the relative time difference between CF (climbing fiber) & PF activation times

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

$\Delta\mathrm{LTD}_{ij}^{(2)}$: 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



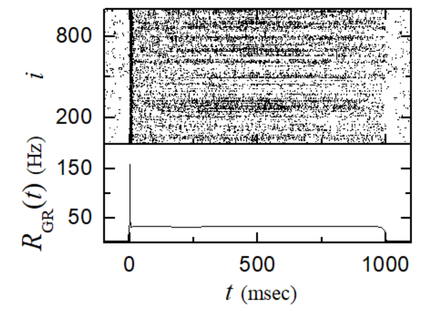
$$\Delta J_{LTD}(\Delta t) = A + B \cdot e^{-[(\Delta t - t_0)/\sigma]^2}$$

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

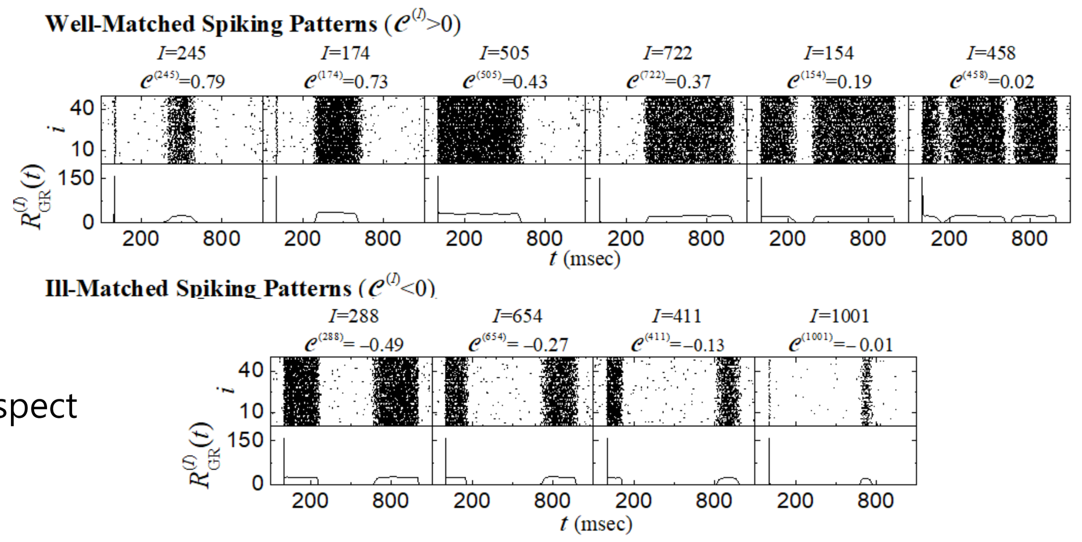
Diverse Spiking Patterns of The GR Clusters

Optimal case: $p_c^* = 0.029$

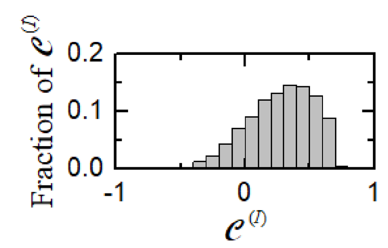
- **Firing Activity in The Whole GR Cells**
  - Raster plot of spikes of 10^3 randomly chosen GR cells:
    Beginning of trial stage: all GR cells fire due to strong transient CS signal
    Remaining part of the trial stage: GR cells make random repetition of transitions between active and inactive states 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
- **Diverse Spiking Patterns in GR clusters**
  - $R_{GR}^{(I)}(t)$: Instantaneous cluster spike rate in the Ith GR cluster
  - Diverse spiking patterns $R_{GR}^{(I)}(t)$: Well- & ill-matched with respect to US $[f_{US}(t)]$

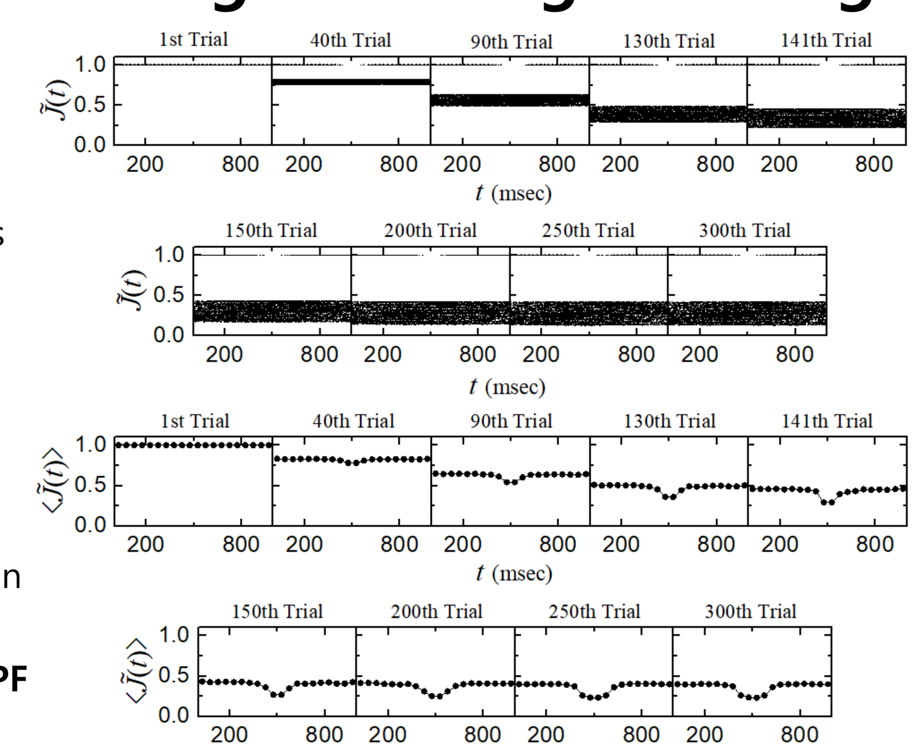


- **Characterization of Diverse Spiking Patterns**
  - Conjunction index $\mathcal{C}^{(I)}$: Cross-correlation between $R_{GR}^{(I)}(t)$ and $f_{US}(t)$ at the zero-time lag
    Well-matched spiking group → $\mathcal{C}^{(I)}>0$
    Ill-matched spiking group → $\mathcal{C}^{(I)}<0$
  - Diversity Degree $\mathcal{D}$: Relative standard deviation of $\{\mathcal{C}^{(I)}\}$
    $\mathcal{D}$=1.842



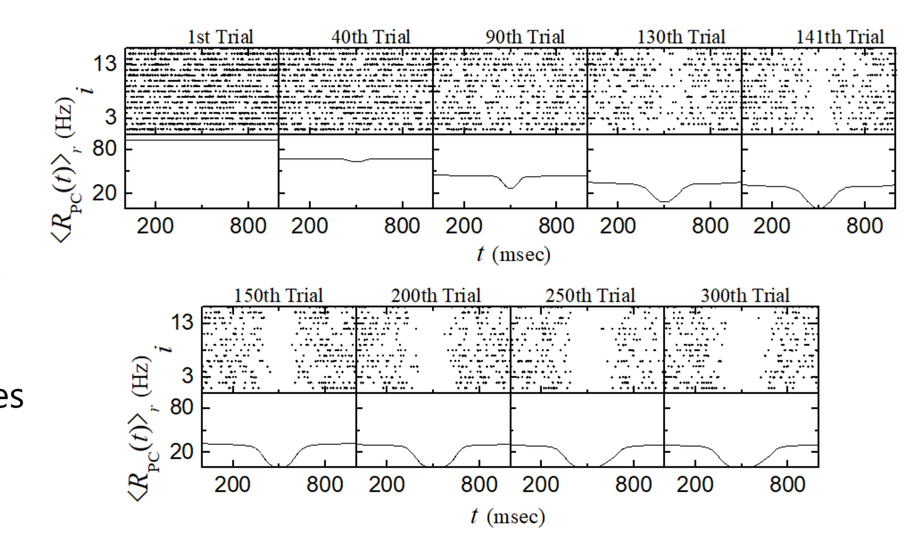
Change in PF-PC Synaptic Weights during Learning

- **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 spiking 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 spiking 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



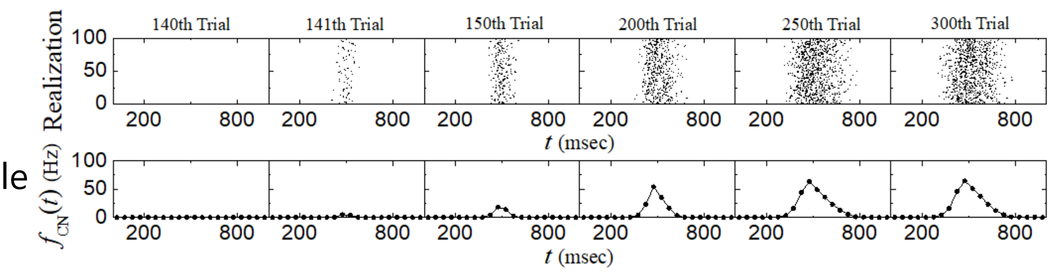
Change in Firing Activity of PCs during Learning

- **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.

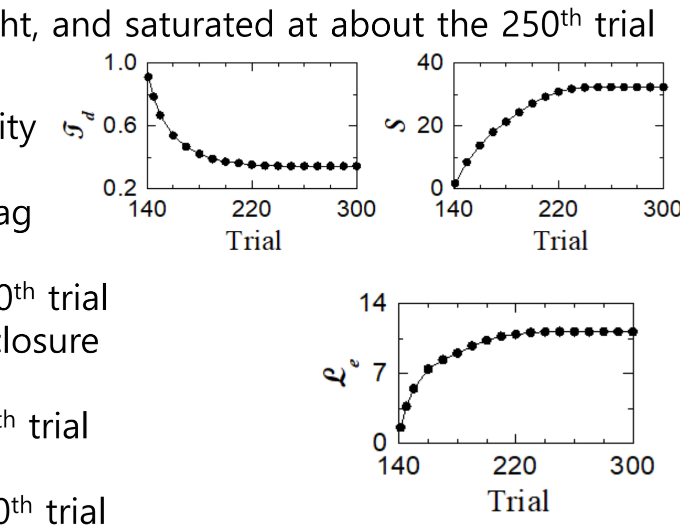


Change in Firing Activity of CN during Learning

- **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 $f_{CN}(t)$: Bell-shaped curve.
    With the trial, increase in bottom-base width and peak height, and saturated at about the 250th trial

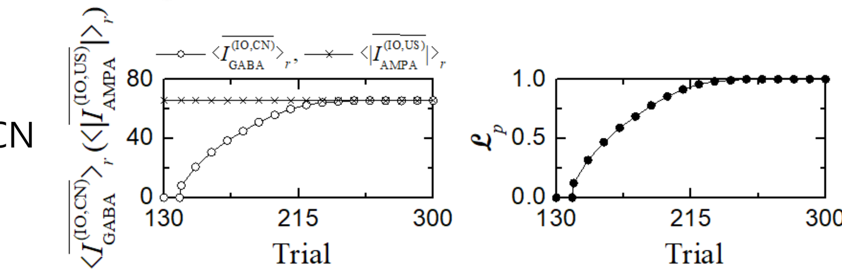


- **Learning Efficiency Degree**
  - Timing degree $\mathcal{T}_d$: Matching degree between the firing activity of CN and US signal
    Cross-correlation between $f_{CN}(t)$ & $f_{US}(t)$ at the zero-time lag
    Reflecting width of the bottom base of the bell curve
    With the trial, decrease in $\mathcal{T}_d$,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

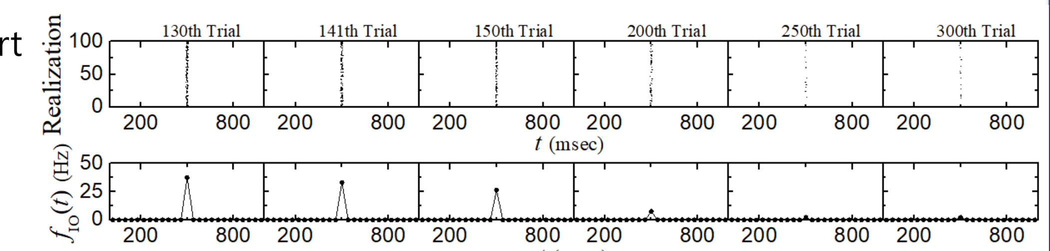


Learning Progress in The IO System

- **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 $\mathcal{L}_p = I_{\mathrm{GABA}}^{(\mathrm{IO,CN})} / \left|I_{\mathrm{AMPA}}^{(\mathrm{IO,US})}\right|$
    With the trial, increase in $\mathcal{L}_p$, and saturated at 1 at about the 250th cycle.

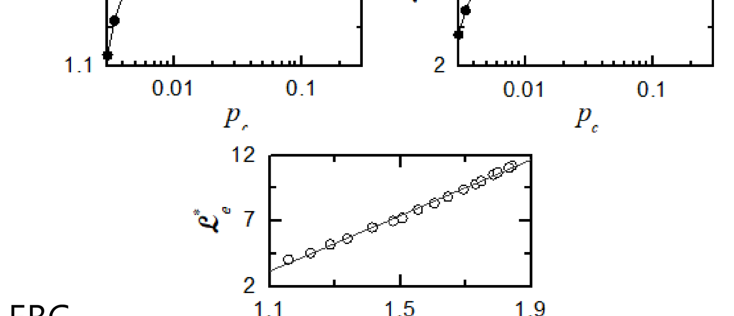


- **Firing Activity of IO neuron during Learning**
  - Before the 141th threshold trial, dense spikes appear in the middle part due to excitatory US signal.
  - With increasing the trial from the threshold, spikes become sparse, because of increased inhibitory input from the CN neuron, and saturated at abut the 250th trial



Relation between Diverse Recoding and Learning Efficiency

- **Diversity Degree ($\mathcal{D}$) & Saturated Learning Efficiency Degree ($\mathcal{L}_e^*$)**
  Bell-shaped curves with maximum at the same optimal value of $p_c^* = 0.029$
- **Strong Correlation between $\mathcal{D}$ and $\mathcal{L}_e^*$**
  The more diverse in temporal recoding of granule cells
  → The more effective in motor learning for the Pavlovian EBC



Summary

- **Diverse Temporal Recoding in The GR clusters**
  Appearance of diverse well- and ill-matched spiking patterns, due to inhibitory coordination of GO cells
  Characterized in terms of conjunction index and diversity degree
- **Effect of Diverse 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 Diverse Recoding and Learning Efficiency Degree**
  Strong Correlation between Diversity Degree $\mathcal{D}$ and Saturated Learning Efficiency Degree $\mathcal{L}_e^*$
  → The more diverse in temporal recoding of granule cells, the more effective in motor learning for the Pavlovian EBC