Characterizing information transmission in cerebellar granule neuron

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***Abstract*— At the cellular scale, single-neurons process information mainly through spikes or action potentials [1]. Although the types of synaptic plasticity and the range of timescales over which they operate suggest that synapses have a more active role in information processing, the parameter space still remains unexplored. We used a mathematical model of cerebellar granule cell to explore information transmission in mossy fibre - granule cell synapse of the cerebellum. The impact of plasticity changes in excitatory synaptic release probability and variation in intrinsic excitability of granule cell was studied combining the modulatory effects of inhibition. We explore the changes in pre and post synaptic factors and report their influence on first spike latency and spike amplitude, revealing the indicators of information encoding in individual neurons [2].**

Keywords- Computational neuroscience, cerebellum, granule cell, information processing.

I. INTRODUCTION

Neural processing can be analyzed in terms of information content, i.e. by quantifying how much information the neural responses convey about the input stimuli [3], [4], [5].To quantify the information transfer of a whole neuron, we focused on a simple neuron cell, the cerebellar granule cell (GC), with which the excitatory input space could be explored extensively (see table XII). MFs (mossy fibres) convey afferent signals to GCs following sensory stimulation [6], [7].

Persistent changes in synaptic strength can cause long term synaptic plasticity, which is supposed to provide the cellular basis for learning and memory and typically takes the form of potentiation (LTP) or depression (LTD)[8], [9], [10].Synaptic plasticity is bidirectional [11] involving the changes in postsynaptic responsiveness or changes in presynaptic neurotransmitter release. Induction of LTP at MF-GC synapses enhances the spike train response of GCs [9]. However, the input-output relationship and quantified output is unknown i.e. how much the information transmitted is changed and how much is transferred through the spike train average frequency, spike correlation, or number of spikes [12]. This knowledge is useful to understanding granular layer computation, which has been proposed to provide temporal dynamics [13], [14] and regulate the input-output relationship through synaptic gain modulation [15], [16] and long-term adaptation [17], [18], [19].

During mossy-fibre granule cell LTP, there is an enhancement in neurotransmitter release and intrinsic excitability of granule cell [20], [9]. LTD expression was associated with a decrease in release probability of the mossy fibre, therefore showing changes opposite to those characterizing LTP [11]. Strong and weak postsynaptic activity determines LTP and LTD respectively. Golgi cells exert an effective time-dependent control over the information conveyed by mossy fibre activity [21].

This paper reports the impact of release probability and intrinsic excitability changes on mossy-fibre granule cell relay and related post-synaptic granule cell response. We also simulated to predict the regulatory effect of Golgi cell inhibition on granule cell firing.

II. METHODS

The granule cell model was adapted from [22] and the simulations were done with the NEURON simulator [23]. Modeling reliability for spiking models was based on the extensive characterization of membrane currents and the compact electrotonic structure of cerebellar granule cells [24], [22].

The release probability of excitatory synapses was varied from 0.1 to 0.8 while keeping the release probability of inhibitory synapses unchanged to study the impacts of plasticity and as a second case the release probability of excitatory synapses were kept unchanged and inhibitory synapse release probability was varied. This was done for various synaptic activation patterns seen in granule cells *in vitro* and *in vivo* in order to understand the effects of release probability changes in granule cell firing. The intrinsic excitability of granule cell was modified and the release probabilities of inhibitory and excitatory synapses were varied to understand the regulatory and modulatory effects of these synapses in granule cell firing.

In vitro like behaviors were studied by giving single spike as input. *In vivo* like behaviors were characterized by burst. Short burst means 5 spikes per burst and long burst means 9 spikes per burst. First spike latency was measured from the time of stimulus to peak of the spike. In all models, the stimulus was applied at t=20ms.

A. Simulating LTP/LTD

By modifying intrinsic excitability and release probability [7] we simulated plasticity in the granule cells. We modified intrinsic excitability by changing ionic current density or gating. We modified the on-off gating characteristics of sodium channel to modify sodium activation and inactivation parameters [28] for higher and lower intrinsic excitability.

III. RESULTS

A. Release probability changes of excitatory synapses affecting MF-GC relay.

During Mossy-fibre (MF) granule cell LTP, an increase in neurotransmitter release was observed [8], [20].

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To understand whether increase in release probability could determine changes in EPSP, the release probability (U) of excitatory synapse was modified from control (U=0.416) while the release probability of inhibitory fibre was set at its control value (U_{inh}=0.34). Various synaptic activation patterns were applied as inputs via MF and for each of the activation patterns, number of spikes; first spike latency (from the peak of the spike) and amplitude of the initial spike were measured. Here, EPSPs were measured from the initial membrane potential of –70mV. With inputs from 4 MF excitatory synapses and 2 inhibitory synapses (see Fig. 1A) single spike was observed and the spike measured 15.52 mV in 23.225 ms under control condition (U=0.416).

When the release probability of the excitatory synapse was increased above 0.416, number of spikes increased, spike amplitude increases and the first spike latency decreased. A decrease in number of spikes was observed when the release probability of excitatory synapse was decreased below 0.416. First spike latency decreased and amplitude increases in all cases (see Table I and Fig. 1A). The same procedure was repeated with other activation patterns (data not shown) comprising combination of excitatory and inhibitory synapses. *In vitro* model behaviour with increased release probability of excitatory synapse was associated with decreased first spike latency, increase in amplitude and increase in number of spikes.

GCs tend to discharge bursts *in vivo* [6]. With input combination of 4MF synapses and 2 inhibitory synapses, *in vivo* model showed 5 spikes, the timing and amplitude of initial spike is 15.55 mV and 23.15 ms respectively under control condition (U=0.416). The release probability of MF synapse was first reduced and then increased from the control condition to study how the changes in release probability of MF synapse affects granule cell firing *in vivo* (Fig. 1B). At U = 0.1 release probability the GC model showed 2 spikes with initial spike amplitude and timing as 9.28 mV and 31.775 ms respectively. Release probability of the excitatory synapse was increased to 0.3, 5 spikes were observed, first spike latency and amplitude measured 14.82 mV and 24 ms respectively. With increase in release probability above 0.416 (control), number of spikes remained unchanged (at 5 spikes), but small changes in spike amplitude and spike timing was observed (see Table II). *In vivo* model with the reduction in release probability of MF synapses below 0.416 (control) was associated with decrease in number of spikes, decrease in spike amplitude and increase in first spike latency. When the release probability was increased above the control (U=0.416), number of spikes remained unchanged and small changes in spike amplitude and spike latency were observed.

TABLE I. VARYING RELEASE PROBABILITY (U) OF MF FOR 4 MF; 2 INHIBITORY SYNAPSES ACTIVE WITH *IN VITRO* LIKE SINGLE SPIKES AS INPUTS

U	Amplitude(mV)	Number of spikes	First spike latency(ms)
0.1	-65.54		
0.3	6.01	1	25.8
0.416	15.52	1	23.225
0.6	16.3	3	22.425
0.8	16.52	4	22.1

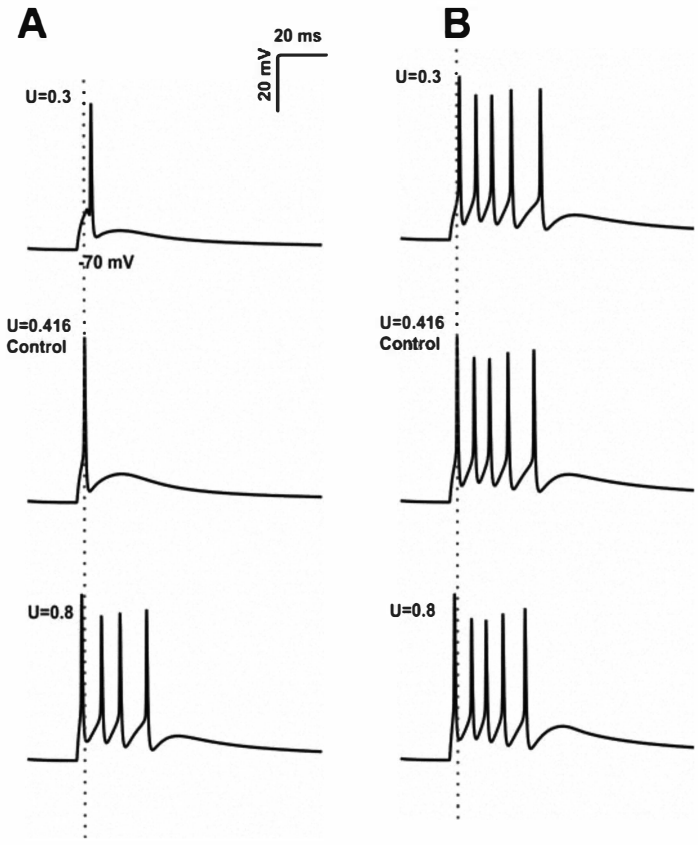

Figure 1. Changes in Mossy fibre release probability. A. EPSP obtained by *in vitro* like input through 4 MF synapses, 2 inhibitory synapses of granule cell with varying release probability. First spike latency was reduced (see the grey dotted line) and number of spikes was increased by the increase in release probability. B. 4 MF synapses, 2 inhibitory synapses activation of granule cell *in vivo* with changes in release probability. At U=0.1, change in initial spike delay and decrease in number of spikes was clearly observed. During control condition (U= 0.416), increase in number of spikes and shortening of first spike latency was seen (the grey dotted line passing through the centre of first spike).When the release probability of excitatory synapses was increased to 0.8, number of spikes remains constant, small change in initial spike latency was seen.

B. Varying inhibition affects LTP

Granule cells showed an increase in intrinsic excitability [25], [8] during LTP. The effect of changes in inhibitory synapse release probability was studied for granule cell with high intrinsic excitability for various synaptic activation patterns. The release probabilities of the Mossy fibre synapses were kept at control value (U = 0.416) for all the activation patterns and the release probability of inhibitory synapses were varied from 0.1 to 0.8.

TABLE II. RELEASE PROBABILITYCHANGES (U) OF MF SYNAPSES FOR INPUTS VIA 4 MF SYNAPSES AND 2 INHIBITORY SYNAPSE *IN VIVO*

U	Amplitude(mV)	Number of spikes	First spike latency(ms)
0.1	9.28	2	31.775
0.3	14.82	5	24
0.416	15.55	5	23.15
0.6	16.26	5	22.425
0.8	16.52	5	22.1

TABLE III. RELEASE PROBABILITY CHANGES OF INHIBITORY SYNAPSE WITH INPUTS VIA 3 MF SYNAPSES AND 2 INHIBITORY SYNAPSES WITH *IN VITRO* LIKE SINGLE SPIKE AS INPUTS.

U_{inh}	Amplitude(mV)	Number of spikes	First spike latency (ms)
0.1	20.0114	1	24.525
0.2	18.832	1	24.525
0.34(Control)	8.84	1	24.65
0.6	14.966	1	24.525
0.8	14.319	1	24.525

To test whether reduction in release probability of inhibitory synapses can favour LTP, the release probability of inhibitory synapse were reduced (U_{inh} < 0.34) from that of control. EPSP-spike complexes by the activation of 2 inhibitory synapses, 3 MF synapses showed that first spike latency and number of spikes are constant (see Table III, Fig. 2 A), but there was a change in spike amplitude (see Table III, Fig. 2C).

The number of Mossy fibre synapses activating granule cell was increased to 4 (2 inhibitory synapses; 4 MF synapses), a spike doublet was observed, but the amplitude and first spike latency remained unchanged (21.758 mV and 23.175 ms respectively) for both release probabilities (0.1 and 0.2).With increased number of MF synapses activating the granule cell, change in spike amplitude, first spike latency and number of spikes was observed when compared with excitation from 3 MF synapses during low levels of inhibition (low release probability of inhibitory synapses and less number of inhibitory synapses) .

The release probability of inhibitory synapses and the number of inhibitory synapses activating granule cell was increased to observe the effects of inhibition on granule cell firing.

At higher release probabilities of inhibitory synapses (0.6, 0.8) 30% reduction in spike amplitude were observed but spike latency and number of spikes remained constant (Table III). To study the effect of increased inhibition the number of inhibitory synapses was increased to 3-4, change in spike amplitude was observed while number of spikes and spike latency remained unchanged.

Increased intrinsic excitability of granule cell caused increase in spike amplitude and decrease in spike latency [9]. Increased intrinsic excitability did not show effects on number of spikes (see Table III). *In vivo* behaviour of granule cell model showed the increase or decrease in release probability of inhibitory synapse did not affect the timing of granule cell firing. Decreased release probability of inhibitory synapses resulted in increased number of spikes, but there was no effect on amplitude or latency (see Table IV, Fig.2 B, D).

TABLE IV. RELEASE PROBABILITY CHANGES OF INHIBITORY SYNAPSES IN A CELL WITH INPUTS VIA 3 MF SYNAPSES AND 2 INHIBITORY SYNAPSES AND WITH *IN VIVO* LIKE BURSTS AS INPUT.

U	Amplitude(mV)	Number of spikes	First spike latency (ms)
0.1	21.11	5	23.95
0.2	21.11	4	23.95
0.34(Control)	14.83	3	24
0.6	21.11	2	23.95
0.8	21.11	2	23.95

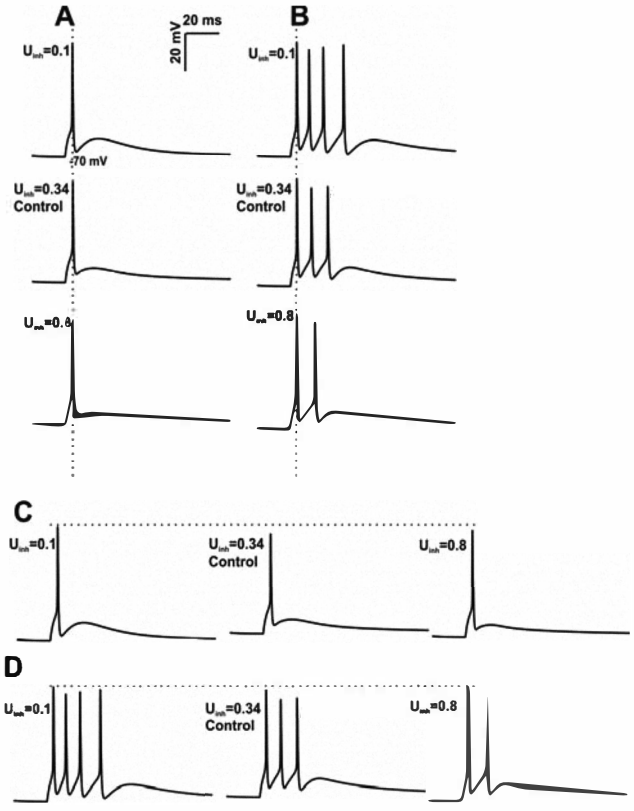

Figure 2. Changes in Inhibitory synapse release probability affecting granule cell firing. A - EPSPs produced by *in vitro* like inputs from 2 inhibitory synapses and 3 MF synapses in granule cell with varying release probabilities of inhibitory synapses. Low and high release probability of inhibitory synapses showed no effect on first spike latency and number of spikes of granule cell. C. The role of intrinsic excitability in spike amplitude was significant. Spike amplitude of granule cell with high intrinsic excitability was higher than in control condition during high and low release probabilities of inhibitory synapses. B, D- EPSPs produced by *in vivo* like activation through 2 inhibitory synapses,3 Mf activation in granule cell with varying release probabilities of inhibitory synapses.

C. Predicting the effects of LTD

Plasticity in MF-GC has been known to be bidirectional [26]. The expression of LTD was associated with decrease in release probability of the excitatory synapses, thereby showing directionally opposite characteristics of LTP [11]. LTD arises due to weak, asynchronous, sporadic activity in pre and postsynaptic neurons [8]. To test effects of LTD induction, intrinsic excitability of the model was reduced and the release probability of MF synapses was reduced below 0.416(control) and its effect in granule cell firing was observed for various synaptic activation patterns. The release probability of inhibitory synapse was kept constant (U_{inh}= 0.34).

With low release probability of MF synapses (U=0.1) *in vitro* granule cell model with low intrinsic excitability did not produce spikes (Fig. 3A). In the presence of low levels of inhibition (0 or 1 inhibitory synapses), and during co-activation of 4 MF synapses, the model produced single spike at U=0.3 release probability.

The effect of low release probability of MF synapses and low intrinsic excitability of *in vivo* granule cell was simulated and studied.

TABLE V. RELEASE PROBABILITY CHANGES (U) OF MF SYNAPSES FOR CELLS WITH *IN VIVO* LIKE INPUTS VIA 4 MF SYNAPSES AND 2 INHIBITORY SYNAPSES.

U	Amplitude(mV)	Number of spikes	First spike latency (ms)
0.1	2.24	2	31.95
0.3	8.59	5	24.075
0.416 (Control)	15.55	5	23.15

When the release probability of MF synapse was increased to 0.3, (U=0.3) number of spikes was increased to 5, first spike latency was decreased while amplitude was increased (Fig. 3B, Table V). *In vivo* like inputs to granule cell model under control condition produced 5 spikes and the initial spike measured 15.55 mV in 23.125 ms.

Low intrinsic excitability of granule cell affected spike amplitude and first spike latency, but it did not show significant effect on number of spikes. Decrease in release probability of MF synapses affects spike latency, number of spikes and spike amplitude. MF-GC LTD was associated with decrease in spike amplitude and increase in first spike latency.

D. Effects of selective inhibition

Inhibition had modulatory effect on granule cell spiking. Spike amplitude was changed significantly when the release probability of inhibitory synapse was increased from 0.1 to 0.8, even though number of spikes and timing was preserved (see Table VI). With increasing release probability in the inhibitory synapses, spike amplitude decreased. This was observed for various combinations of inhibitory and excitatory synapses.

For *in vivo* like inputs, amplitude and latency of the first spike remained unchanged (see Table VII). Golgi cells regulate the induction of long-term synaptic plasticity at the mossy fibre–granule cell synapse. The main output from Golgi cells to granule neurons is GABAergic and inhibits the granule cells [27].

The spike amplitude and first spike latency remained constant for all release probabilities of inhibitory synapses for any particular combination of excitatory-inhibitory synapses. Inhibition did not affect first spike latency during burst like *in vivo* inputs along MF and inhibitory synapses (see Fig. 4 B). For single spike (as seen *in vitro*) inputs along excitatory and inhibitory synapses, varying inhibition (both number of active inhibitory synapses and varying inhibitory release probabilities) regulated spike amplitude (see Fig. 4 A).

TABLE VI. VARIATION OF SPIKES (*IN VITRO*) WITH INHIBITORY RELEASE PROBABILITIES..

U_{inh}	Amplitude (mV)	Number of spikes	First spike latency (ms)
0.1	11.31	1	24.625
Control (0.34)	3.76	1	24.675
0.8	-1.59	1	24.625

a. Spike count and spike latency remained constant or without significant change. 3 MF synapses and 4 inhibitory synapses with *in vitro* like single spike was given as inputs.

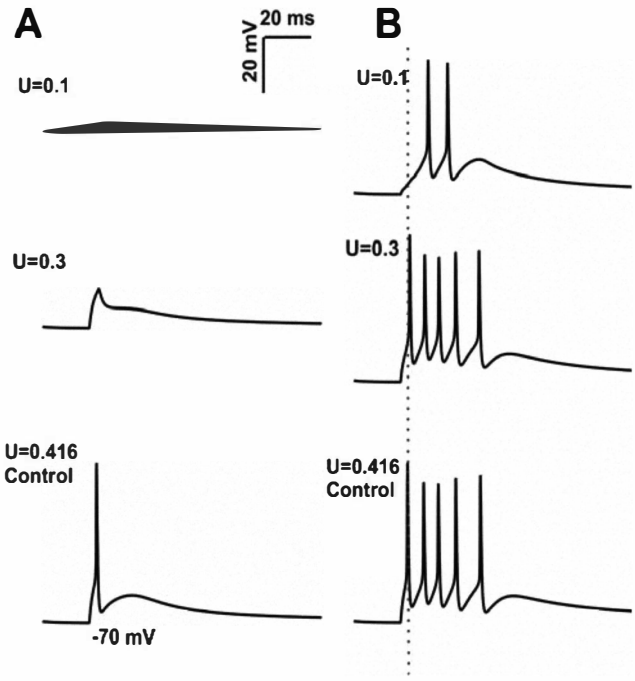

Figure 3. Simulations of changes in mossy fibre release probability and intrinsic excitability. A. *In vitro* behaviour of granule cell model with low release probabilities of MF synapses B. *in vivo* behaviour of granule cell model during low release probability of mossy fibre. First spike latency was increased when there was a reduction in MF synapse release probability coupled with low intrinsic excitability of granule cell (see grey dotted line passing through control). It can be noted that the decrease in release probability of MF synapses was associated with decrease in number of spikes.

E. Release Probability Changes during LTP

During LTP, granule cells show an increase in intrinsic excitability and enhanced neurotransmitter release [25], [8], [20]. Combining variations in intrinsic excitability, the effect of increase in excitatory synapse release probability was studied for various combinations of excitatory and inhibitory synapses. To test the effects of increase in mossy fibre release probability during LTP, the release probability of excitatory synapse was increased (U>0.416) from control. As release probability was changed with the same synaptic pattern (4 excitatory synapses and 1 inhibitory synapse activating the cell), number of spikes increased (Table VIII, Fig. 5A).

Spike count and spike latency remained constant or without significant change. 3 MF synapses and 4 inhibitory synapses with *in vivo* like single spike as inputs activated the granule neuron.

TABLE VII. VARIATION OF SPIKES (*IN VIVO*) WITH INHIBITORY RELEASE PROBABILITIES.

U_{inh}	Amplitude (mV)	Number of spikes	First spike latency (ms)
0.1	14.83	4	24
Control(0.34)	14.83	1	24
0.8	14.83	1	24

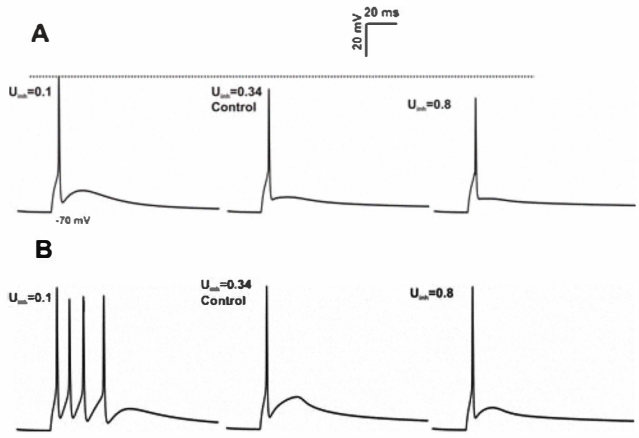

Figure 4 - Effect of inhibition on spike amplitude A. 4 inhibitory synapses, 3 excitatory synapses activation of granule cell with varying the release probability of inhibitory synapse for single spike input. Increase in the release probability of inhibitory synapse cause the reduction in spike amplitude (see the grey dotted line).B. EPSP produced by burst like input through 4 inhibitory synapses, 3 excitatory synapse in granule cell. *In vivo* behaviour showed significant changes not in amplitude but in number of spikes.

In vivo behaviour of granule cell model showed, when the release probability of MF was increased above the control (U=0.416), number of spikes remained constant and small variations in spike amplitude and first spike latency was observed but the increase in intrinsic excitability caused an increase in spike amplitude (see Table IX, Fig. 5 B).

F. Impacts of inhibition during LTD

Variation of inhibitory release probability with low intrinsic excitability was studied for various synaptic activation patterns. The release probability of the Mossy fibre synapses were kept at control value (U = 0.416) for all the activation patterns and the release probability of inhibitory synapses were varied from 0.1 to 0.8.

TABLE VIII. SPIKING PROPERTIES FOR SINGLE SPIKE INPUT VIA MF, INHIBITORY SYNAPSES DURING LTP.

U	Amplitude (mV)	Number of spikes	First spike latency (ms)
Control(0.416)	15.52	2	23.225
0.6	21.788	3	22.4
0.8	21.637	4	22.075

a. 4 excitatory synapses and 1 inhibitory synapses provide inputs to the granule cell. Note the change in latency and increase in number of spikes and amplitude.

TABLE IX. SPIKING PROPERTIES FOR BURST INPUT VIA MF, INHIBITORY SYNAPSES DURING LTP.

U	Amplitude (mV)	Number of spikes	First spike latency (ms)
Control (0.416)	15.55	6	23.125
0.6	21.725	6	22.4
0.8	21.635	6	22.075

a. No change was observed in number of spikes but significant changes are seen in first spike latency.

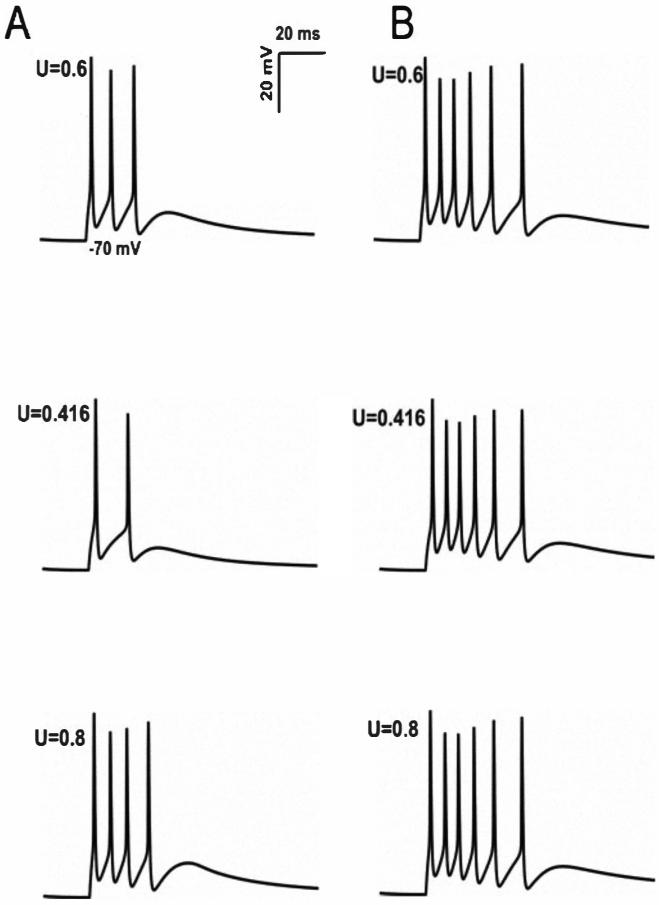

Figure 5. Simulating LTP A. 1 inhibitory synapse 4 excitatory synapses activating a granule cell with high intrinsic excitability. Varying release probability of mossy fibre for single spike input shows difference in number of spikes A. Single spike input via MF B. Burst like input via MF. Note the number of spikes remains constant.

Bi-directional nature of plasticity [26] was noticed as inhibitory strengths increased. *In vitro* like behavior of granule cell model with increased inhibition and low intrinsic excitability showed delayed spike timing and change in spike amplitude. When inhibition was predominant (both in number of synapses and release probability change), the granule cell did not generate spikes (See Table X, Fig. 6A).

TABLE X. SPIKING PROPERTIES FOR SINGLE SPIKE INPUT VIA 3 MF SYNAPSES, 4 INHIBITORY SYNAPSES DURING LTD.

U_{inh}	Amplitude (mV)	Number of spikes	First spike latency (ms)
0.1	3.61	1	24.775
Control (0.34)	3.76	1	24.675
0.8	-14.24	0	25.15

a. Note the decrease in spike amplitude

TABLE XI. SPIKING PROPERTIES FOR BURST INPUT VIA 3 MF SYNAPSES, 4 INHIBITORY SYNAPSES DURING LTD

U_{inh}	Amplitude (mV)	Number of spikes	First spike latency (ms)
0.1	8.624	4	24.05
Control(0.34)	14.83	1	24
0.8	8.531	1	24.05

For bursts of spikes as input, number of spikes remained unchanged with higher release probabilities (see Table XI, Fig. 6B) both spike latency and amplitude tend to remain unchanged while number of spikes increases when inhibition is lowered.

G. *Modulation of spiking during plasticity*

To understand the information encoding in terms of number of spikes and spike latency [2], we explored the parameter space of mossy fibre excitations and spatial inhibition for granule cell under control, LTP and LTD conditions. Absence of inhibition sets the upper limit of spikes in case of control, LTP and LTD simulations. As inhibition increased slight decrease in number of spikes was observed. Intrinsic excitability mainly modulated the first-spike latency in most patterns. Higher intrinsic excitability reduced first spike delay (see Fig. 7). The study (Fig. 7 for *in vitro* single spike input) revealed how LTP/LTD with inhibition could influence granule neuron information flow.

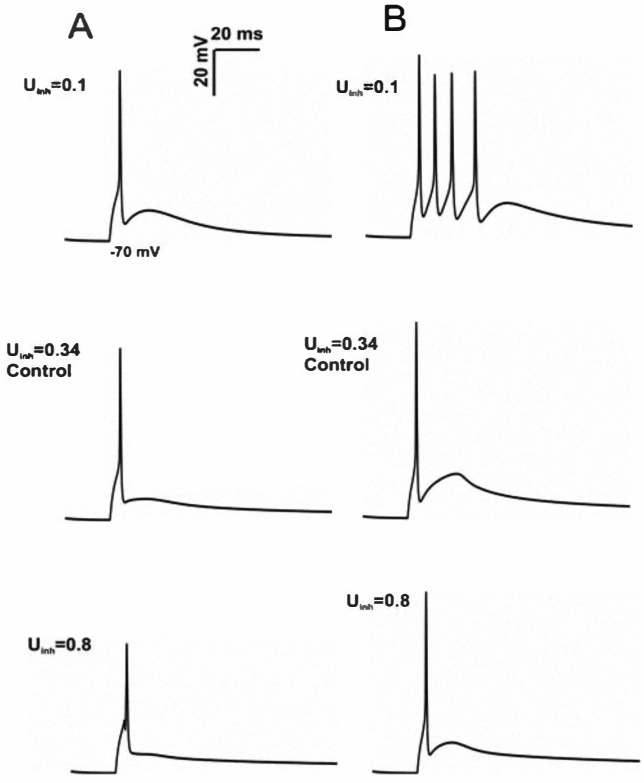

Figure 6. Spiking characteristics of granule cell with single and burst as input. For *in vitro* like behaviour first spike delay was reduced with lesser inhibition. The first spike delay remains constant irrespective of the release probability change in inhibitory synapses for in vivo like behaviour.

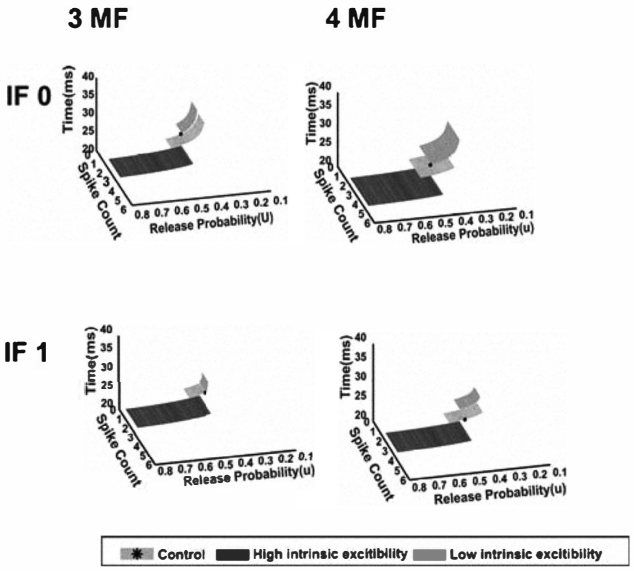

Figure 7. Quantifying information transfer in spiking neurons for single spike (*in vitro*) input. Light grey region shows number of spikes, first spike delay for release probability changes (U=0.35-0.45). Black dot (over light grey) shows the control (U=0.416) value. Black area shows model variation with high intrinsic excitability. The grey area shows model with low intrinsic excitability. X axis indicated various release probabilities; Y-axis shows number of spikes, Z-axis shows first spike latency (ms). MF: Mossy Fiber Synapses, IF: Inhibitory Fibre.

A similar observation with *in vivo* like inputs was observed (data not shown). However, in case of in vivo data there was a sharper modulation by intrinsic excitability and hence the variation in number of spikes.

TABLE XII. COMBINATORIAL SYNAPTIC ACTIVATION PATTERNS AND SPIKING CELL.

***A** in vitro*

		Excitatory Synapse			
		1 MF	2 MF	3 MF	4 MF
Inhibitory Synapse	IF 0	0	0	1	2
	IF 1	0	0	1	2
	IF 2	0	0	1	1
	IF 3	0	0	1	1
	IF 4	0	0	1	1

***B** in vivo*

		Excitatory Synapse			
		1 MF	2 MF	3 MF	4 MF
Inhibitory Synapse	IF 0	0	3	5	7
	IF 1	0	2	4	6
	IF 2	0	0	3	5
	IF 3	0	0	2	4
	IF 4	0	0	1	3

a. A- shows the number of spike obtained for single spike input to combinations of excitatory and inhibitory synapses. B shows the number of spike data for granule cell burst input. MF: Mossy Fibre Synapses, IF: Inhibitory Fibre.

IV. DISCUSSION

This paper provides extensive analysis of information transmission in granule neuron. The input-output parameter space analysis beyond current experimental techniques has been explored. Part of information is transmitted as rate, part as time precision and that high correlation among the MF inputs was characteristic of most informative stimuli. Importantly, the transmitted information was regulated by inhibition especially during induction of LTP and LTD.

In vivo simulations of granule cell showed that increase in the release probability of MF synapses alone does not make significant changes in firing and yet a decrease in MF synapse release probability can reduce granule cell firing.

Coupling the increase in release probability of MF synapses with high intrinsic excitability of the granule cell (as seen during LTP) showed an enhancement in firing properties of cerebellar granule cell. Increase in release probability and intrinsic excitability of granule cell showed increases in spike amplitude and decrease in spike latency whereas firing frequency remains same [9]. During low release probabilities of MF synapses, number of spikes is reduced compared to control.

In vitro granule cell behaviour showed that the changes in release probability of the inhibitory synapse did not affect granule cell firing or first spike latency whereas considerable impacts were observed in the amplitude of spikes. Release probability changes in inhibitory synapses coupled with high intrinsic excitability showed the same effect. Changes in number of spikes and first spike latency were not significant. Increased intrinsic excitability of granule cell combined with low release probability in inhibitory synapses affected spike amplitude.

In vivo granule cell model with decreased release probability of inhibitory synapses affected granule cell firing whereas no significant change was noticed on spike amplitude and timing. Combined with high intrinsic excitability changes, inhibitory synapse release probability variations showed spike amplitude changes due to the effect of intrinsic excitability. Little or low release probability of inhibitory synapses may enhance firing of granule cell.

Low intrinsic excitability in granule cell showed changes in spike amplitude and first spike latency, but it did not show significant effect on number of spikes. Decrease in release probability of MF synapses along with low intrinsic excitability affected the spike latency, number of spikes and spike amplitude. MF-GC LTD is associated with decrease in spike amplitude and increase in first spike latency. The change in number of spikes was not significant.

Low intrinsic excitability in granule cell combined with high release probability of inhibitory synapses showed a decreased number of spikes and decreased spike amplitude, but the spike latency was preserved. Low release probability of inhibitory synapses showed increased number of spikes, with low spike amplitude due to low intrinsic excitability.

Theoretical network models predict that information in the MF-GC relay is a relevant parameter that could optimize cerebellar performance for certain tasks and under appropriate learning rules [17] [19]. Hence, plasticity at this relay may be an important element of tremendous storage capacity in the learning of coordination of actions, sensorimotor or cognitive, in which the cerebellum participates.

Given the pervasiveness of temporal information in external stimuli and the generality of the time-dependent mechanisms studied in the current paper, all temporal responses needed for forming coarse temporal code can be stipulated. This, in turn, will help estimate overall behaviour in firing in the underlying granular layer network. Also selective inhibition in GC may help to quantify and to reveal mechanisms of coincidence detection and spatial pattern separation as described in Motor learning theory [15].

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