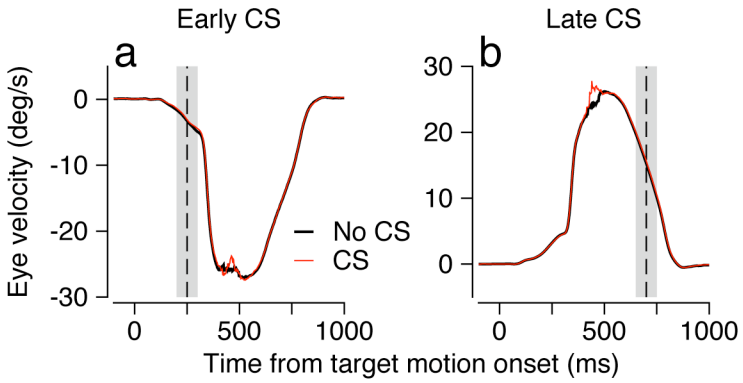
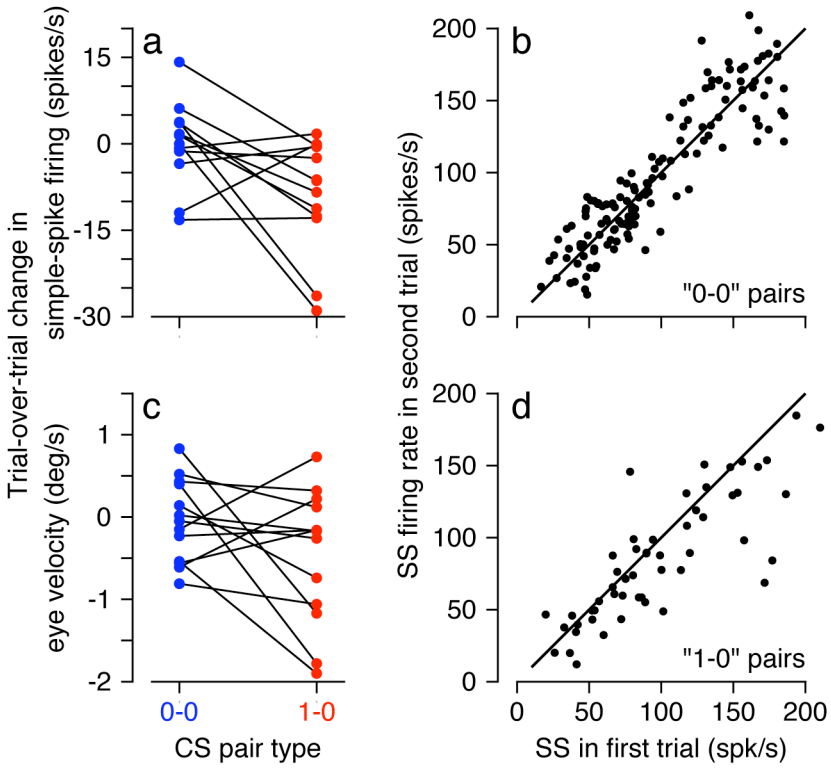
***On-line Supplementary Material***

Links from complex spikes to local plasticity and motor learning in the cerebellum of awake-behaving monkeys

Javier F. Medina and Stephen G. Lisberger




**Supplementary Figure 1.** Comparison of the average eye velocity in learning trials with versus without complex spike responses. a) Data from off-direction learning trials based on analysis of events surrounding the instructive change in target direction that occurred at the vertical dashed line. b) Data from on direction learning trials surrounding the offset of target motion, at the vertical dashed line. The similarity of the red and black traces shows that any difference in the sensory stimulus was miniscule, and therefore could not be the determinant of whether or not a Purkinje cell emitted a complex spike on a given trial.




**Supplementary Figure 2.** Summary of the trial-over-trial changes in simple spike firing rate and eye velocity for individual Purkinje cells and individual trials for off-direction learning. **a, c**: Each symbol shows the average trial-over-trial change over the entire analysis interval. Blue and red symbols show measurements for "0-0" and "1-0" trials and black lines connect the blue and red symbols from each individual Purkinje cell. The trial-over-trial change in simple spike firing rate in **a** was reduced for "1-0" versus "0-0" pairs in 8 Purkinje cells, was unchanged in 4 Purkinje cells, and was increased in one Purkinje cell. Paired t-tests indicated that the trial-over-trial changes in simple spike firing were statistically significant across the population of Purkinje cells ($p<=0.013$, $n=13$ Purkinje cells). Trial-over-trial changes in eye velocity were not statistically significant in **c** ($p=0.129$). **b, d**: Comparison of simple spike firing rate in the analysis interval for the second and first trial of "0-0" pairs (**b**) and "1-0" pairs (**d**). Each symbol shows measurements from a single trial and the graphs pool data across Purkinje cells. Data for single pairs of "1-0" trials tended to plot below the unit line, indicating that the firing rate tended to be lower on the second versus the first trial in "1-0" pairs. Thus, the data from analysis of individual Purkinje cells and trials substantiate the findings in the population averages. Interestingly, Purkinje cells from both groups 1 and 2 were among those with substantial trial-over-trial depression of simple spike responses, implying that the learning-related increase in simple spike response during off-direction learning in group 2 Purkinje cells results from weak activation of complex spike inputs by the instructive change in target direction rather than from some deficiency in cellular plasticity in their input pathways.

***Supplementary Appendix***

The relationship between the large trial-over-trial depression of simple spike firing and the much smaller trial-over-trial depression of eye velocity can be understood in terms of the different meaning of the neural and behavioral measures. The trial-over-trial change in simple spike response ($\Delta SS_i$) is a local event in the $i^{th}$ Purkinje cell, namely the one under study. It is linked to the occurrence of a complex spike in that Purkinje cell on the first of a pair of trials. The trial-over-trial change in eye velocity is a global event determined by the average of the trial-over-trial changes in simple spike firing across a population of *N* Purkinje cells:

$$\Delta\dot{E} = \left( \frac{1}{N} \sum_{i=1}^{N} \Delta SS_i \right) \frac{1}{\bar{s}} \tag{1}$$

Dividing the average change in simple spike firing rate in *spikes/s* by the average sensitivity to eye velocity across the population measured during visually guided pursuit in *spikes/s per deg/s* ($\bar{s}$) converts the right side of the equation to the same units as the left side, eye velocity in *deg/s*.

Next, consider the analysis in Figure 6c, which asked whether the trial-over-trial change in eye velocity was different when there was a complex spike in the first of a pair of trials compared to when there was not. In terms of Equation (1), we measured the difference in the trial-over-trial change in eye velocity depending on whether or not there was a complex spike on the Purkinje cell under study in the first of two consecutive learning trials:

$$\delta(\dot{E} \mid CS) = \Delta\dot{E}_{1-0} - \Delta\dot{E}_{0-0} \tag{2}$$

Here $\Delta\dot{E}_{1-0}$ and $\Delta\dot{E}_{0-0}$ are the trial-over-trial changes in eye velocity for a "1-0" pair and a "0-0" pair, which depend on the distribution of changes in simple spike firing across the full population of Purkinje cells, and not merely on the change in simple spike firing of the Purkinje cell under study. The relationship between what happens in the Purkinje cell under study and the rest of the population will depend on the degree of synchronization between the complex spike under study and those in all other Purkinje cells. We assume that some fraction ($f_{CS}$) of Purkinje cells emit a complex spike when the Purkinje cell under study does ("1-0" pairs), and that the rest of the Purkinje cells ($1\text{-}f_{CS}$) emit a complex spike when the Purkinje cell under study does not ("0-0" pairs); to simplify the equations, we also assume that $\Delta SS_i$ is equal to the constant $\Delta SS$ for all Purkinje cells that have "1-0" pairs and is zero for all Purkinje cells with "0-0" pairs. Then Equation (2) becomes:

$$\delta(\dot{E} \mid CS) = \frac{f_{CS}\Delta SS}{\bar{s}} - \frac{(1 - f_{CS})\Delta SS}{\bar{s}} \tag{3}$$

Here, the trial-over-trial change in eye velocity on "1-0" pairs of trials is determined by the fraction of Purkinje cells with complex spike responses linked to that in the cell under study while the change in eye velocity on "0-0" pairs is determined by the remainder of the Purkinje cells, whose complex spike responses occur when there is not a complex spike (i.e. a "0-0" pair) in the Purkinje cell under study. Algebra reduces Equation (3) to a simple linear relationship:

$$\delta(\dot{E} \mid CS) = \frac{(2f_{CS} - 1)\Delta SS}{\bar{s}} \tag{4}$$

Equation (4) predicts that there should be no difference between the "1-0" and "0-0" pairs in the trial-over-trial change in eye velocity if $f_{CS}=0.5$, because half the Purkinje cells emit a complex spike and undergo depression of simple spike responses on "1-0" trials for the Purkinje cell under study and the other half on"0-0" trials for the Purkinje cell under study. If $f_{CS}=1$, meaning that on any given trial all Purkinje cells emit a complex spike, or none do, then there should be a large trial-over-trial change in eye velocity to go with the change in simple spike firing rate across the population of Purkinje cells.

We can go one step further and reorganize Equation (4) to predict the relationship between the average trial-over-trial change in simple spike response measured in the Purkinje cell under study and the trial-over-trial change in eye velocity that we measure at the same time:

$$\frac{\Delta SS}{\delta(\dot{E} \mid CS)} = \frac{\bar{s}}{(2f_{CS} - 1)} \tag{5}$$

Equation 5 defines the ratio: the complex spike-contingent change in simple spike firing divided by the complex spike-contingent change in eye velocity. If complex spike responses are synchronized across all Purkinje cells ($f_{CS} = 1$), then this ratio should be the same as measured during pursuit of visual target motion ($\bar{s}$). With this in mind, we return to Figure 3 and estimate that the sensitivity to eye velocity of Group 1 Purkinje cells is approximately 2.5 for the eye movement learned through a change in the direction of target motion. From Figures 6 and 7, we estimate that the sensitivity to eye velocity is approximately 15 for the analysis of trial-over-trial changes. A six-fold enhancement in sensitivity to eye velocity is predicted by Equation (5) when $f_{CS} = 0.58$: 58% of Purkinje cells would emit a complex spike on the same trials as the Purkinje cell under study while 42% would emit a complex spike when the Purkinje cell under study does not.

The foregoing analysis implies that there is a small tendency toward synchrony across the population of IO cells that drive complex spike responses during pursuit learning, but does not require that the population emit an all-or-nothing complex spike response as a group. The model represented by Equations (1)-(5) is a simplification of the real situation. For example, it assumes that there will be no trial-over-trial increase in simple spike firing for a "0-0" pair. Still, the model serves to show that the trial-over-trial changes in simple spike firing rate and eye velocity needn't be inextricably linked, and that their ratio puts some bounds on the tendency for synchrony of complex spike responses within a given Purkinje cell population. Even if there is a more complex dynamic relationship among complex spike responses across the population, the same general conclusions would hold with somewhat different quantitative predictions for the degree of synchronization.