

Coordination of visually guided movements requires a transformation from planned kinematics to executed dynamics that must be learned through trial and error. Thus motor adaptation may be mediated by adjusting the computations performed by brain regions that include primary motor cortex (M1) and dorsal premotor cortex (PMd) [1]. Previous studies have shown that M1 neurons are highly responsive to dynamic perturbations such as viscous force fields [2]. In contrast to M1, whose activity is closely related to the dynamics of movement, PMd is believed to be involved in movement planning in kinematic coordinates [3]. The differing functional roles of M1 and PMd in coordinating movement suggest different roles in motor adaptation.

To investigate the role of PMd in motor learning, we compared neural activity during adaptation to either visual rotation (VR) or viscous curl force field (CF) perturbation. A macaque monkey was trained to make visually-guided reaches by using a planar manipulandum to maneuver a computer cursor into a target that moved to a series of random locations (Figure 1A). Each experimental session consisted of three epochs: a 15-minute baseline period, a 35-minute adaptation period with either VR or CF perturbation, and a 25-minute washout period when the perturbation was removed (Figure 1B). The viscous CF produced forces at 85 degrees to the direction of movement with a viscosity constant of 0.15 Ns/cm (Figure 1C). The visual rotation was a static 30-degree counter-clockwise rotation of the mapping between hand and cursor movement (Figure 1D). The CF affected only the dynamics of the movement, and when fully adapted, the kinematic trajectories were identical to the unperturbed reaches. In contrast, the VR perturbed the kinematics of the intended movement.

To show adaptation, we isolated movements between targets and computed mean curvature of hand position in a sliding two-minute window (Figure 2). When the perturbation was applied, the curvature increased in the negative direction (since the force field and rotation acted in the counter-clockwise direction) then gradually moved towards baseline. When the perturbation was removed, curvature increased in the opposite direction, the so called “after-effect”.

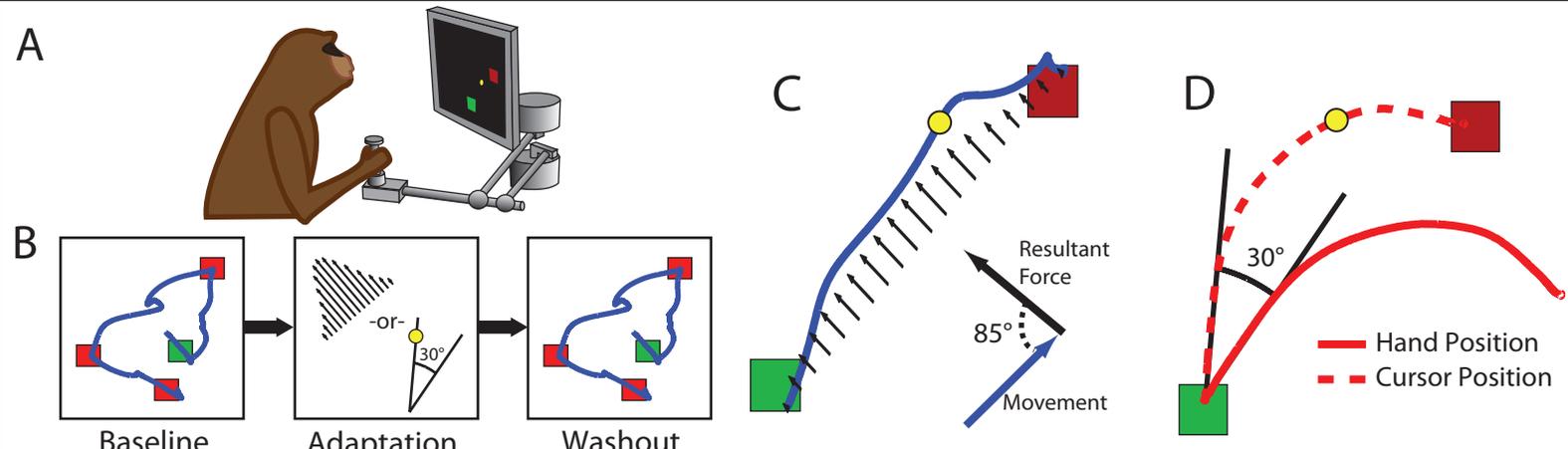
We recorded extracellular action potentials using a 96-channel microelectrode array (Blackrock Microsystems, Salt Lake City, Utah) implanted in PMd of one monkey (Figure 3A). We described the spatial tuning of each cell using a preferred direction (PD), or the direction of hand movement for which the cell fires maximally. To compute PDs, we defined a window extending 300ms before and 200ms after the time of peak velocity. We computed movement direction and mean firing rate within the window, the latter offset by 100 milliseconds to account for neural transmission delays. We binned the movements into 45 degree bins and fit a cosine function relating firing rate to movement direction using a bootstrapping analysis with 1000 iterations to compute the mean PD and 95% confidence bounds. We considered a cell to be significantly tuned if the sinusoidal regression had  $R^2 > 0.2$  and the confidence bounds were less than  $\pm 15$  degrees. Any cell that did not meet these criteria was excluded from further analysis.

We defined a change in tuning if the PD confidence bounds under the test condition did not overlap those of the reference condition. “Adapting cells” had a shifted PD late in the adaptation period relative to baseline, and returned to the baseline in washout. We divided the adaptation period into two halves and compared neural tuning in the early and late phases of learning. The CF and VR had markedly different effects on neural behavior in these periods. In the early phase of CF adaptation, the majority of PMd cells (~70%) exhibited a change in PD (Figure 4C). The PDs of the population shifted in the direction of the field (Figure 4B, blue histogram). However, in the late phase most of these cells returned to their baseline tuning even though the field was still active. In contrast, while few PMd cells (~20%) were adapting in the early phase of VR adaptation, most (~60%) exhibited a significant change in tuning in the late phase. With a VR of +30°, the final hand endpoint is -30° from the target location. Since we computed tuning with respect to actual movement direction and not target direction, the change in PD is opposite of the direction of rotation. In the washout period, virtually all of the cells returned to their baseline tuning.

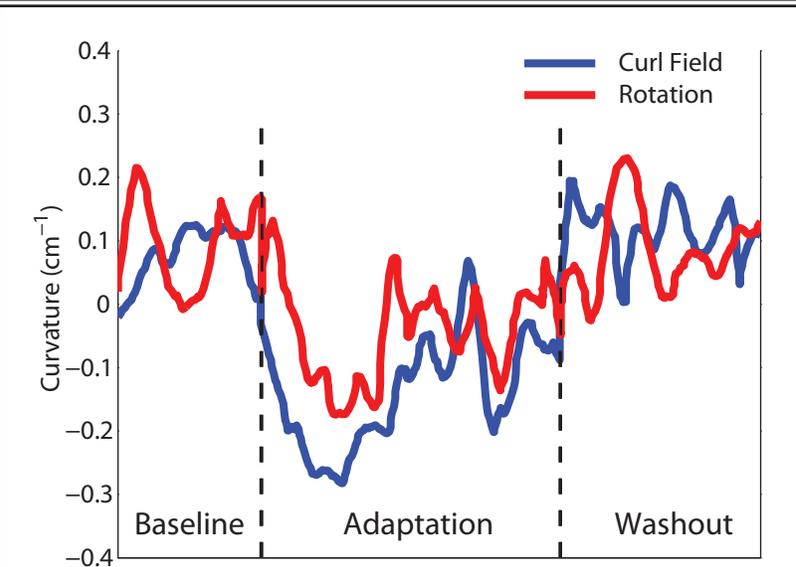
In contrast to M1, which has previously been shown to represent adaptation to the viscous force field [2], we found that most cells in PMd did not reflect adaptation to this perturbation. Instead, PMd encodes the kinematics of the task. The spatial tuning curves used here represent the mapping between neural discharge and hand movement. A shift in PD suggests a change in this mapping. The force field immediately changed the relationship between discharge and movement by actively pushing the hand, leading to a change in the tuning of the PMd cells in the early phase of adaptation. Since the CF does not change the kinematics of the task, the majority of these cells return to their original tuning as the monkey adapts. The visual rotation, on the other hand, did not alter the relationship between neural discharge and movement. Consequently, the neural tuning did not change in the early phase of adaptation and the PDs only began to shift as the monkey adapted to the kinematic perturbation. Together, these results suggest that adaptation to a kinematic perturbation is reflected in the activity of PMd neurons.

#### References

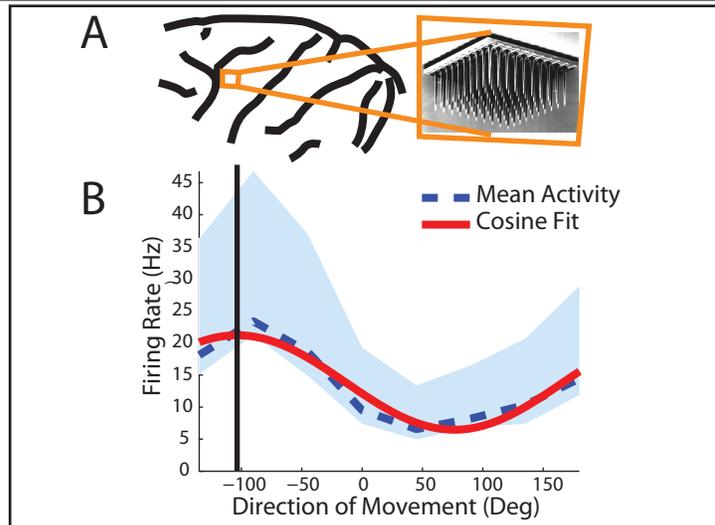
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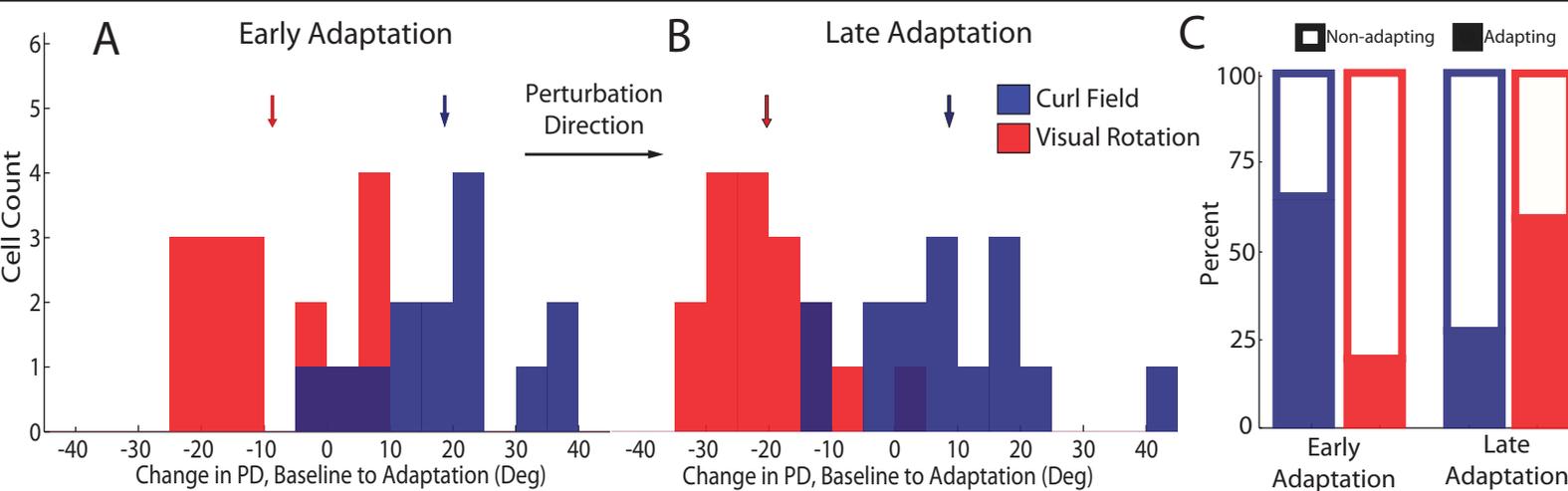
**Figure 1. Behavioral task.** (A) A monkey performed a random movement task using a manipulandum to control a displayed cursor. (B) Each session consisted of three task epochs: a baseline period of unperturbed movements to compute baseline neural tuning, a prolonged period of adaptation to one of two perturbations, and finally a “washout” period to reassess the neural behavior. (C, D) The perturbation was either a viscous curl force field (CF) with a constant of 0.15 Ns/cm applied at 85 degrees from the direction of movement or a static visual rotation (VR) of 30 degrees between the hand movement and the cursor movement. Each session used only one perturbation type.



**Figure 2. Adaptation to the perturbations.** Movement curvature averaged over a sliding two minute window for both the CF task (blue) and VR task (red). The perturbation increased the curvature magnitude at the start of the the adaptation period. Curvature gradually decreased as the monkey adapts and increased in the opposite direction due to after-effects when the perturbation was removed.



**Figure 3. Neural recordings and directional tuning.** (A) Neurons were recorded using microelectrode arrays implanted in dorsal premotor cortex (PMd). (B) Mean firing rate of a representative PMd neuron as a function of movement direction (blue line) with 95% confidence bounds (shaded blue area). Each neuron was described with a cosine tuning curve relating firing rate to the direction of limb movement (red line) to extract a preferred direction of movement (black vertical line).



**Figure 4. Changes in neural tuning during adaptation.** (A) Distribution of PD changes for the PMd neurons between baseline period and early phase of the adaptation period for the CF (blue) and VR (red) sessions. Arrows indicate the mean of each distribution. In this early phase of adaptation, the PMd cells have a greater shift in PD with the CF than the VR (CF mean: 18.9°, VR mean: -8.56°). (B) Neural PD changes between baseline period and late phase of the adaptation period. Here, the VR causes a greater shift in PDs (CF mean: 8.67°, VR mean: -20.4°). (C) Comparison of the number of cells that adapted to each perturbation in the early and late phases. Cells whose PD was significantly different in the adaptation period compared to the baseline are “adapting” cells. In the early phase (left), most cells adapted with the CF but few adapted to the VR. In the late phase (right), the majority of cells adapted to the VR and most cells returned to baseline tuning in CF.