The transfer function of the rhesus macaque oculomotor system for small-amplitude slow motion trajectories

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Abstract

Two main types of small eye movements occur during gaze fixation: microsaccades and slow ocular drifts. While microsaccade generation has been relatively well-studied, ocular drift control mechanisms are unknown. Here we explored the degree to which monkey smooth eye movements, on the velocity scale of slow ocular drifts, can be generated systematically. Two male rhesus macaque monkeys tracked a spot moving sinusoidally, but slowly, along the horizontal or vertical directions. Maximum target displacement in the motion trajectory was 30 min arc (0.5 deg), and we varied the temporal frequency of target motion from 0.1 to 5 Hz. We obtained an oculomotor "transfer function" by measuring smooth eye velocity gain (relative to target velocity) as a function of frequency, similar to past work with large-amplitude pursuit. Monkey eye velocities as slow as those observed during slow ocular drifts were clearly target-motion driven. Moreover, like with large-amplitude smooth pursuit, eye velocity gain varied with temporal frequency. However, unlike with large-amplitude pursuit, exhibiting primarily low-pass behavior, small-amplitude motion tracking was band-pass with the best ocular movement gain occurring at ~0.8-1 Hz. When oblique directions were tested, we found that monkey oblique pursuit gain for small-amplitude slow motion trajectories was >1. Our results provide a catalogue of the control abilities of the monkey oculomotor system for slow target motions, and they also support the notion that smooth fixational ocular drifts are controllable. This has implications for neural investigations of drift control and the image-motion consequences of drifts on visual coding in early visual areas.

Introduction

Small fixational eye movements continuously move the retinal image, even though they never deviate the center of gaze (or fovea) away from objects of interest. Such continuous movements mean that the neural signals representing input images in a variety of early visual areas are continuously modulated, and this has implications for theoretical interpretations of neural variability across trials, as well as population correlations in simultaneously recorded neurons (McFarland et al. 2016; Rucci and Victor 2015). Therefore, understanding the neural control mechanisms for fixational eye movements is an important first step towards understanding the full impact of these eye movements on neural coding, and ultimately visual perception.

Fixational eye movements come in two main flavors: microsaccades, which are rapid gaze shifts that look like big saccades; and smooth ocular drifts, which are slow changes in eye position occurring in between microsaccades (Barlow 1952; Murphy et al. 1975; Nachmias 1961). Even though microsaccades have received a substantial amount of research attention recently (Hafed 2011; Hafed et al. 2015; Krauzlis et al. 2017; Rolfs 2009), drifts remain to be relatively underexplored. For example, the mechanisms for generating ocular drifts are unknown, whereas microsaccade generation has been studied in a variety of different brain areas (Arnstein et al. 2015; Hafed et al. 2009; Hafed and Krauzlis 2012; Peel et al. 2016; Sun et al. 2016; Van Horn and Cullen 2012). Moreover, uncovering detailed neural mechanisms for microsaccade generation in certain key brain areas was instrumental for uncovering important, previously unappreciated, consequences of these eye movements on vision, perception, and even cognition (Chen et al. 2015;

Hafed 2013; 2011; Hafed et al. 2015; Krauzlis et al. 2017; Tian et al. 2016; Veale et al. 2017). Thus, exploring the neural mechanisms for slow ocular drift generation is a worthwhile effort, especially given the fact that during fixation, microsaccades are brief events in an otherwise continuous sea of ocular drifts.

Here, towards approaching that ultimate goal, we aimed to characterize the degree to which the control system for eye position in the macaque monkey brain is able to generate very slow smooth pursuit eye movements, on the velocity scale of fixational ocular drifts. In other words, is it possible for monkeys to volitionally generate a slow eye movement that is as small in amplitude and velocity as slow ocular drifts, but that is clearly controlled and with a predictable motion trajectory? We designed behavioral experiments motivated by potential analogies that one can make between slow ocular drifts and smooth pursuit eye movements (Cunitz 1970; Martins et al. 1985; Nachmias 1961), similar to analogies that one makes between microsaccades and larger saccades (Hafed 2011; Krauzlis et al. 2017). After all, smooth pursuit eye movements are (relatively) slow rotations of the eyeball, similar in nature to slow ocular drifts, and the circuits for generating such smooth pursuit eye movements are well studied (Krauzlis 2004).

We presented macaque monkeys with small-amplitude sinusoidal target trajectories, and we asked how well their small-amplitude slow eye movements can track such trajectories. Our approach was to assume that for the frequency ranges that we studied, the oculomotor system may behave, to a first approximation, like a linear system. This

means that we can present a single frequency and measure the response, and then test another frequency, and so on. The gain and phase lag of tracking at each frequency can thus allow estimating an "equivalent" transfer function of the oculomotor system (Ohashi and Mizukoshi 1991). Previous attempts like this with larger-amplitude (and faster) eye movements in smooth pursuit were effective, and showed that pursuit tracks very well for low frequencies (<1 Hz), but that it then behaves relatively poorly with higher frequencies (exhibiting both lower gain and larger phase lag) (Bahill and McDonald 1983; Collewijn and Tamminga 1984; Fabisch et al. 2009; Martins et al. 1985; Ohashi and Mizukoshi 1991; Rottach et al. 1996). We were interested in what happens in the monkey with much smaller and slower eye movements. The key comparison was to see whether controlled slow eye movements as slow as fixational ocular drifts would be possible. Critically, we performed our experiments on monkeys in order to demonstrate that these animals are instrumental for ultimately uncovering the neural control mechanisms for slow ocular drifts, and also in order to complement earlier human work on the topic (Cunitz 1970; de Bie and van den Brink 1986; Martins et al. 1985; Murphy et al. 1975; Nachmias 1961; Wyatt and Pola 1981).

Materials and Methods

Animal preparation and laboratory setup

We recorded eye movements from two male rhesus macaque (macaca mulatta) monkeys (monkey A and monkey M) aged 6-7 years. We implanted one eye (left for monkey A and right for monkey M) in each animal with a scleral search coil for eye tracking using the magnetic induction technique (Fuchs and Robinson 1966; Judge et al. 1980). Surgical procedures for implantation were similar to those described earlier (Chen and Hafed 2013; Hafed and Ignashchenkova 2013), and the experiments were approved by ethics committees at the regional governmental offices of the city of Tübingen. These experiments were in accordance with European Union guidelines on animal research, as well as the associated implementations of these guidelines in German law.

We used monkeys in this study for two important reasons. First, the monkeys had scleral search coils implanted, which allowed the most precise measurement of small-amplitude slow eye movements, including fixational drifts. Video-based eye trackers (used in most human studies) are less reliable than scleral search coils for measuring slow eye movements. Second, and more importantly, the monkeys are now being used in neurophysiological recording experiments, such that direct neural correlates of our observations here can be identified and disseminated; particularly to complement earlier human work on similar questions (Cunitz 1970; de Bie and van den Brink 1986; Martins et al. 1985; Murphy et al. 1975; Nachmias 1961).

During data collection, the animals were seated in a primate chair 73 cm from a CRT computer monitor in an otherwise dark room. The monitor had a pixel resolution of 34 pixels/deg and a refresh rate of 120 Hz. Stimuli were presented over a uniform gray background (29.7 Cd/m^2 in Experiment 1, and either 29.7 or 4.4 Cd/m^2 in Experiment 2). A small white spot (~5 x 5 min arc square) having 86 Cd/m^2 luminance in Experiment 1 and either 86 or 48.1 Cd/m^2 in Experiment 2 was used as the moving target for smooth pursuit eye movements (see *Behavioral tasks* below).

Graphics on the CRT monitor were presented by a computer running Matlab's Psychophysics Toolbox (Brainard 1997; Kleiner et al. 2007; Pelli 1997). This computer in turn received commands from a real-time I/O system from National Instruments (Austin, USA), which ensured control of the display on a frame-by-frame basis, as well as real-time monitoring of animal behavior and reward. The system was described recently (Chen and Hafed 2013; Tian et al. 2018; 2016).

Behavioral tasks

Experiment 1: Temporal frequency series

The monkeys fixated a small white spot for 350-550 ms at trial onset, after which the spot started moving either horizontally or vertically along a sinusoidal position trajectory of only 30 min arc (0.5 deg) amplitude. The monkeys had to track this moving target with their eyes, and target position in deg (along either the horizontal or vertical axis) could be described by the following equation

$$target\ position = 0.5 \times \sin(2\pi f t + \varphi) \quad (1)$$

where f is the temporal frequency of target trajectory, t is time from motion onset, and ϕ could be either 0 or π across trials. The temporal frequency, f, of target motion was chosen randomly from trial to trial from among the following values: 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.8, 1, 2, 3, 4, or 5 Hz. Target motion duration was constant within a session, but could vary across sessions in the range of 3000-4200 ms, depending on animal motivation on any one day. In all cases, we had a long enough target motion duration to ensure that we were analyzing steady-state tracking behavior, even for the smallest values of f (associated with the slowest target position changes). Horizontal and vertical target trajectories were collected in different blocks of trials, and we analyzed a total of 867 trials from monkey A and 1392 trials from monkey M. We did not penalize the monkeys (e.g. by aborting trials) for making catch-up saccades as long as they stayed within a radius of ~1-1.5 deg around the instantaneous target position.

Experiment 2: Amplitude series

The monkeys performed a similar experiment to that described above, but this time, the temporal frequency, f, was maintained at 0.5 Hz. Also, we interleaved different target motion directions, and we varied the amplitude of the target motion. Target motion trajectory was now described by the following equations

$$horizontal\ target\ position = Amp_h \times \sin(2\pi f t) \quad (2)$$

$$vertical\ target\ position = Amp_v \times \sin(2\pi f t) \quad (3)$$

where f was fixed at 0.5 Hz, and Amp_h and Amp_v specified the target motion amplitudes. For purely horizontal target motions, Amp_h and Amp_v were chosen to result in radial amplitudes of 0.25, 0.5, 1, or 2 deg. We also introduced two oblique directions: "+45 deg oblique pursuit" was used to describe the case when Amp_h and Amp_v were equal and positive (again from among 0.25, 0.5, 1, or 2 deg); "+135 deg oblique pursuit" was used to describe the case when Amp_v had an opposite sign from Amp_h and Amp_h was negative (e.g. -0.25 deg for Amp_h and +0.25 deg for Amp_v). In other words, the two oblique directions both started with upward motion trajectory, but with one first moving rightward/upward (+45 deg) and the other first moving leftward/upward (+135 deg). During the sessions, we interleaved all amplitude and direction conditions. We analyzed a total of 969 trials from monkey A and 2145 trials from monkey M.

Experiment 3: Fixation comparison

For a subset of analyses, we compared eye velocity during tracking of small-amplitude motion trajectories to eye velocity during fixation. The monkeys simply fixated the same small spot for 1000-1400 ms before getting rewarded. We analyzed a total of 3160 trials from monkey A and 5222 trials from monkey M.

Data analysis

Detecting catch-up saccades

We detected catch-up saccades using velocity and acceleration criteria (Chen and Hafed 2013; Hafed et al. 2009; Krauzlis and Miles 1996), and we manually inspected all

movements to correct for misses or false detections. For a subset of the data, we used instead a novel state-of-the-art machine-learning approach for saccade detection using convolutional neural networks, which we have developed (Bellet et al. 2018).

Catch-up saccade detection was necessary for performing focused analyses on smooth pursuit eye movements (see below), but we also analyzed interesting properties of these saccades themselves. For example, we explored both the frequency of occurrence and amplitude of these eye movements as a function of either target motion temporal frequency, f, or amplitude (Amp_h, Amp_v).

Measuring smooth pursuit gain and phase lag

We plotted eye velocity as a function of time for either horizontal or vertical eye movements. For oblique motion trajectories (Experiment 2), we performed a coordinate rotation such that one component of eye velocity was along the motion trajectory and the other was orthogonal, and we plotted eye velocity for the component along the motion trajectory (in other analyses, we also analyzed the horizontal and vertical components of oblique eye velocity independently). We then picked a period of steady-state smooth pursuit execution by excluding the first 1000 ms of eye movement data after target motion onset (in Experiment 2, we relaxed this to 300 ms). In each velocity trace, we then excised any interval during which a catch-up saccade was being executed, and we also removed 10 ms before and 10 ms after each such saccade. The data that were excised were replaced by Not-a-Number (NaN) labels, such that averages of eye velocity across

242 trial repetitions of a given condition did not include the large velocity transients
243 associated with catch-up saccades.
244
245 After plotting saccade-free eye velocity from any one trial, we fitted the resulting curve,
246 using a least-squares fitting algorithm, with a sinusoidal function (of appropriate temporal
247 frequency for the condition) in which the amplitude and phase values of the sinusoid
248 were the fitting parameters. This resulted in a population of amplitudes and phases from
249 the fitting procedure across trial repetitions of a given condition. For example, for 0.5 Hz
250 horizontal target trajectories in Experiment 1, we could have a population of *N* fitted
251 gains or phase lags across trials. We then summarized these *N* values into the mean gain
252 or mean phase lag at 0.5 Hz target motion temporal frequency, and with appropriate 95%
253 confidence intervals. "Gain" was defined as the ratio of the fitted eye velocity amplitude
254 in a sinusoid divided by the true amplitude of the target velocity sinusoid. For example,
255 for *f* Hz horizontal target trajectory with Amp_h deg position amplitude in equation 1 above
256 (and also equations 2 and 3), the target velocity amplitude was $2\pi f Amp_h$. Similar
257 procedures were performed for all conditions. In all analyses, we had >25 trials per
258 condition in each animal (most often, significantly more; e.g. see Fig. 2).
259
260 In a subset of analyses (e.g. Fig. 9), we measured eye velocity directly. For example, we
261 estimated eye velocity during smooth pursuit initiation or during baseline fixation (before
262 target motion onset). We defined a measurement interval of 50 ms, starting either at -100
263 ms or +100 ms from motion onset. The earlier interval measured eye velocity during

fixation, whereas the latter interval measured eye velocity during smooth pursuit initiation.

Spectral analysis of eye positions

For some analyses of the data from Experiment 1, we performed a discrete Fourier transform decomposition of eye position traces from the different values of f in equation 1. We picked, in each trial, an epoch of steady-state smooth pursuit (i.e. removing the initial component immediately after motion onset as described above) that was 2500 ms long. We then applied a Hanning window followed by discrete Fourier transformation to investigate whether low-gain tracking was still modulated by the temporal frequency of the target motion. We then plotted the average spectrum across the individual trial spectra.

In all figures presented in this paper, we designated 95% confidence intervals as error bars, such that the statistical robustness of our results can be easily assessed.

Results

Band-pass tuning for small-amplitude slow motion tracking in the monkey

Our goal was to systematically characterize the quality of monkey ocular control when tracking small-amplitude slow motion trajectories. We were motivated by the more general question of how slow ocular drifts that occur during gaze fixation may be controlled, and how similar such control may be to the control needed when volitionally tracking a moving target. We therefore asked two monkeys to pursue a small spot that moved sinusoidally with an amplitude of only 30 min arc (0.5 deg) and different temporal frequencies (Experiment 1; Material and Methods). For temporal frequencies of <1 Hz, the peak velocities of target motion (based on equation 1) were always <3.14 deg/s, and they were even smaller for even lower frequencies like 0.4 Hz, and also at off-peak-velocity epochs of tracking. Therefore, the target velocities involved in our experiments were similar in scale to the velocities with which the eye may drift on its own during steady fixation (Cherici et al. 2012; Martins et al. 1985).

We found that eye velocity always tracked the temporal frequency of the target, albeit to varying degrees of success. For example, Fig. 1A shows average saccade-free (Materials and Methods) eye velocity from monkey M when this monkey tracked a horizontally moving spot at 0.4 Hz in Experiment 1. Error bars denote 95% confidence intervals across trials, and the solid blue line shows the true target velocity (based on the derivative of equation 1). As can be seen, the eye moved sinusoidally at a similar temporal frequency to the target, but eye velocity gain was quite low; fitting a sinusoid to the eye velocity data (in the sustained pursuit interval; Materials and Methods; red line in Fig 1A)

showed a peak velocity amplitude in the fit of 0.532 deg/s relative to the true target peak velocity of 1.26 deg/s, resulting in a gain of only 0.4235. There was also a phase lead of ~90 ms, which amounted to a lead of 0.036 of a full cycle of motion trajectory (3.6% of a full cycle). When the target temporal frequency was 0.8 Hz instead, eye velocity gain was significantly better (Fig. 1B), but it then decreased once again for even higher frequencies (e.g. Fig. 1C; temporal frequency of 2 Hz). Phase lead or lag also matched the gain changes by progressively shifting towards larger and larger lags, with 0.8 Hz showing now a minimal phase delay (28 ms, or 0.022 of a full cycle) in tracking (as opposed to a lead at 0.4 Hz), and the higher frequency showing an even more substantial delay of 35 ms or 0.07 of a full cycle. Therefore, monkey smooth ocular tracking of small-amplitude slow motion trajectories may be described as being band-pass in nature, unlike the classic description of smooth pursuit tuning (with much faster target speeds) as being low-pass (Collewijn and Tamminga 1984; Fabisch et al. 2009; Rottach et al. 1996). This difference is not due to the use of monkeys in our current study, as opposed to humans in the earlier ones, because monkeys are indeed capable of high-gain sinusoidal pursuit of foveal spots when faster target speeds (but similar low temporal frequencies) are used (Hafed et al. 2008; Hafed and Krauzlis 2008). It is very intriguing to us, nonetheless, that very highly trained human subjects performed significantly better at low temporal frequencies than our monkeys when face with similar small-amplitude motions (Martins et al. 1985).

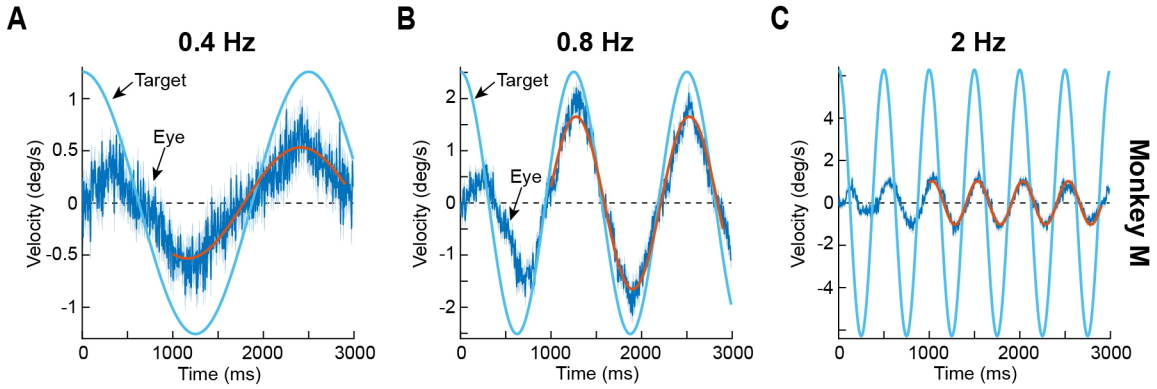

Figure 1 Band-pass nature of monkey smooth pursuit of small-amplitude slow motion trajectories. (**A**) Example tracking behavior from monkey M with 0.4 Hz sinusoidal target motion. The solid blue sinusoid represents target velocity. The dark blue data plot shows mean eye velocity across trials (surrounded by 95% confidence interval bands in a fainter color). The red sinusoid is a fit of the eye velocity data in a sustained interval starting 1000 ms after target motion onset. As can be seen, the eye tracked the frequency of target motion well, but with a markedly low peak velocity (i.e. low gain). (**B**) Tracking gain was significantly higher at 0.8 Hz. This panel is formatted identically to **A**. (**C**) For even higher frequencies, pursuit gain decreased again, as evidenced by the much smaller amplitude of the sinusoid describing eye velocity relative to that describing target velocity (red and blue sinusoids, respectively). Note that phase lag also increased (compare the phase of the solid red and blue sinusoids in each panel). Error bars, when visible, denote 95% confidence intervals.

We confirmed the band-pass nature of small-amplitude slow motion tracking in our two monkeys, and also with both horizontal and vertical tracking. For each temporal frequency, *f*, in equation 1 (Materials and Methods), we estimated the gain of pursuit (similar to Fig. 1; Materials and Methods) and plotted it for horizontal and vertical tracking, along with 95% confidence intervals (Fig. 2A). In both monkeys, pursuit gain peaked at ~0.8-1 Hz, and this happened for both horizontal and vertical tracking, although vertical tracking always had significantly worse pursuit gain than horizontal tracking (Rottach et al. 1996). For a frequency of 0.1 Hz, pursuit gain in both monkeys seemed to increase relative to, say, 0.2 Hz and 0.3 Hz. This was because at 0.1 Hz, the target was barely moving with a peak speed of only 0.314 deg/s. At such speeds, the monkeys seemed to rely much more on saccades than slow eye movements to correct eye

position errors (e.g. see Fig. 5A), and their own fixational ocular drifts were significantly faster than the target motion (e.g. see Fig. 3A). Therefore, for all frequencies other than 0.1 Hz, we observed a band-pass characteristic of monkey smooth pursuit gain for small-amplitude slow motion trajectories.

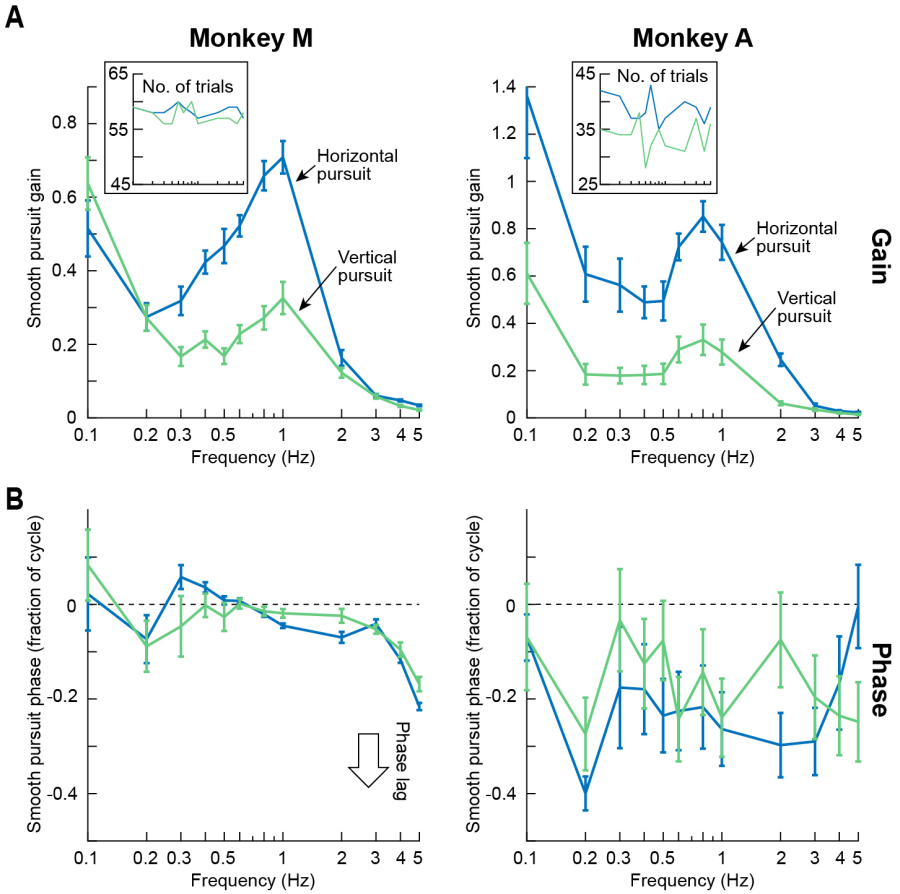

Figure 2 Band-pass nature of slow motion smooth pursuit in both monkeys. (**A**) Each panel shows the gain of smooth pursuit (i.e. the ratio of red sinusoid amplitude to blue sinusoid amplitude in Fig. 1) as a function of target motion frequency. The left panel shows data from monkey M, and the right panel shows data from monkey A. Error bars denote 95% confidence intervals, and the insets indicate the number of trials per condition used for analysis. As can be seen, pursuit gain peaked at around 0.8-1 Hz for both monkeys, and was lower for both lower and higher frequencies. In both animals, pursuit gain seemed high at 0.1 Hz; at this frequency, the target was barely moving and ocular drift velocities could be substantially higher than target velocities (Martins et al. 1985). Also, in both animals, pursuit gain was significantly worse for vertical tracking as opposed to horizontal tracking. (**B**) A similar analysis but now for pursuit phase (e.g. the phase difference between the red and blue sinusoids of Fig. 1). In monkey M, higher frequencies were associated with larger phase lags. This dependence of phase lag on frequency was not so evident in monkey A, for which an overall lag existed even at low frequencies. Note that the phase lag is displayed here as a fraction of a cycle. Thus, a constant temporal lag would translate into a larger fraction with increasing frequency (see text). All error bars indicate 95% confidence intervals.

We similarly analyzed pursuit phase lag, reporting it as a fraction of a full cycle (Fig. 2B); that is, a constant temporal delay in phase would mean a larger fraction of a cycle with increasing frequencies. In monkey M, this was the case: higher target motion frequencies resulted in progressively more and more pursuit lag when represented as a fraction of a full cycle. However, this was less so in monkey A, for which there was an overall lag in pursuit that was independent of frequency. The insets in Fig. 2A show the total numbers of trials analyzed for each condition.

Therefore, for both horizontal and vertical smooth pursuit eye movements, tracking of very slow motion trajectories in monkeys is seemingly different from classical experiments with faster target speeds; for the small-amplitude slow motions, pursuit efficacy at low frequencies is significantly impaired, and only recovers at ~0.8-1 Hz. For larger target speeds, evidence from the literature shows that smooth pursuit typically exhibits low-pass behavior, with high gain at all low frequencies up to ~1 Hz (Collewijn and Tamminga 1984; Fabisch et al. 2009; Hafed et al. 2008; Hafed and Krauzlis 2008; Martins et al. 1985; Rottach et al. 1996). As stated above, in highly trained humans, such a low-pass behavior of smooth pursuit seemed to also still persist for small-amplitude target trajectories like the ones that we used (Martins et al. 1985); perhaps this difference from our monkey results is due to extensive training of the humans to avoid making catch-up saccades.

392 *Controllability of monkey ocular velocities as slow as those during fixational ocular*
393 *drifts*
394 Despite the low gain of smooth pursuit at low temporal frequencies in Figs. 1, 2, eye
395 velocity in our monkeys was still clearly controllable. For example, sinusoidal tracking
396 was still evident at 0.4 Hz even with the reduced gain (Fig. 1A). As stated earlier, we
397 were interested in this phenomenon particularly because the velocities with which
398 tracking occurred at these low temporal frequencies seemed similar to the velocities with
399 which ocular drifts during fixation normally take place. For example, peak target velocity
400 at 0.1, 0.2, and 0.3 Hz was 0.314, 0.628, and 0.942 deg/s, respectively, which are all
401 within the range of eye velocity during fixational ocular drifts (Cherici et al. 2012;
402 Martins et al. 1985). To confirm this, we collected control fixation data from the same
403 animals. In these trials, the spot never moved, and the monkeys simply fixated it for
404 approximately 1000 ms (Materials and Methods). We measured eye velocity during
405 microsaccade-free fixation epochs, and we related them to the peak eye velocity at each
406 temporal frequency during tracking (Fig. 3A). Specifically, in Fig. 3A, we plotted the
407 same data as in Fig. 2A but now as raw measurements of peak eye velocity instead of as
408 gain values. We then plotted the average velocities observed during gaze fixation
409 (horizontal lines), again along with 95% confidence intervals. At the lowest and highest
410 tracking frequencies (e.g. 0.1-0.2 Hz or 4-5 Hz), peak eye velocity during pursuit of slow
411 motion trajectories was significantly lower than eye velocity during fixation (error bars in
412 Fig. 3A denote 95% confidence intervals). However, the eye was still well-controlled
413 because gain was not zero (Fig. 2A). We also further confirmed this by analyzing the
414 frequency spectrum of eye position traces for different temporal frequencies (particularly

415 the small ones associated with the slowest peak velocities). We found that there was a
416 peak in the power spectrum of eye position traces near the frequency with which the
417 target was moving (Fig. 3B). This means that eye position had a harmonic component
418 that was close in frequency to that present in the target motion trajectory even at the low
419 gain values observed in Fig. 2A. Finally, we also inspected example eye position traces
420 for low (Fig. 3C) or high (Fig. 3D) tracking frequencies, and clear modulation of
421 saccade-free eye position was still present (e.g. see the gray arrows in Fig. 3C, D).
422 Therefore, slow ocular movements at velocities similar to or lower than the velocities of
423 slow fixational ocular drifts are relatively well-controlled in this behavior (Wyatt and
424 Pola 1981).
425

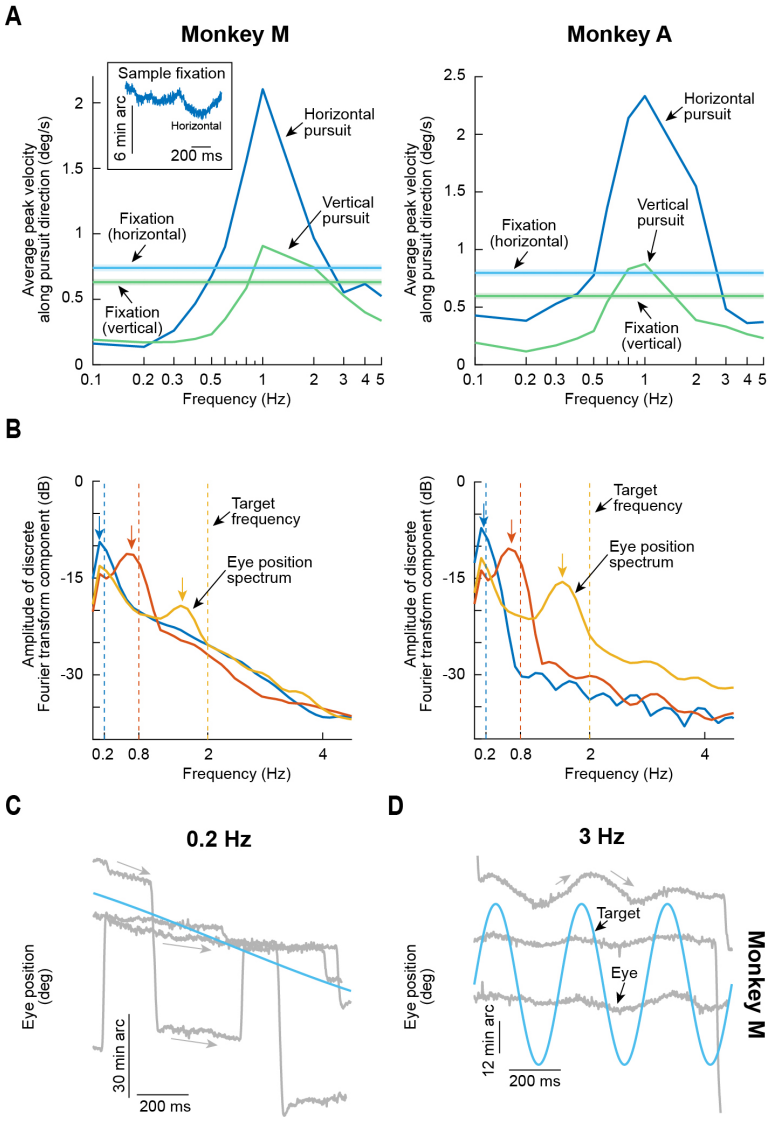

Figure 3 Monkey ocular velocities as slow as those during fixational drifts occurred during smooth pursuit of slow motion, but they were still systematically controlled to track the motion trajectory. (**A**) The curves show the same data as in Fig. 2A, but this time as real measurements of peak eye velocity as opposed to a gain ratio. The solid horizontal lines show average eye velocity during fixation (Materials and Methods), surrounded by 95% confidence intervals (the inset shows an example 1-second fixational eye position trace, demonstrating how ocular drift has substantial non-zero eye velocity even with a stationary fixation spot). Fixational drift velocity was higher than pursuit peak velocities at pursuit frequencies of, say, 0.2 Hz, 0.3 Hz, and 4 Hz. This means that eye velocities as slow as those during ocular drifts are controllable by the central nervous system of the monkey. (**B**) This idea is supported by analyzing the spectral content of eye position traces for different pursuit target frequencies. Even at very low frequencies (e.g. 0.2 Hz and 0.8 Hz) associated with low pursuit velocities (as in **A**), eye position still exhibited a peak in the spectrum at a frequency near target motion. This indicates that eye position was still following target motion (even if at low gain). (**C**, **D**) Sample 1-second eye position traces (shown in gray) from three example trials at 0.2 Hz (**C**) or 3 Hz (**D**), both of which exhibited very weak pursuit gain (**A** and Fig. 2). In both cases, eye position was systematically controlled to follow target trajectory (e.g. see the gray arrows). Thus, monkeys are capable of slow control of their drift velocities in our task.

Dependence of monkey catch-up saccade frequency and amplitude on temporal frequency

Our results so far have focused on smooth eye velocity effects. However, we also analyzed and catalogued catch-up saccade frequency and amplitude. We found that catch-up saccades behaved in different ways for temporal frequencies higher or lower than the frequency associated with peak smooth pursuit gain (~0.8-1 Hz). For example, in Fig. 4A, we plotted the frequency of catch-up saccades as a function of temporal frequency in Experiment 1. In both animals, catch-up saccade frequency reached a peak at the same temporal frequency for which smooth pursuit gain was maximum. This suggests that eye position was continuously adjusted with both smooth pursuit and saccadic eye movements when overall tracking was particularly effective (i.e. with high gain). Catch-up saccade frequency then dropped dramatically for higher temporal frequencies, but this drop was not so dramatic for lower temporal frequencies. This suggests that for the lower temporal frequencies, when the spot was barely moving, catch-up saccades played a role more similar to that of fixational microsaccades: they optimized eye position on the target on average (Guerrasio et al. 2010; Ko et al. 2010; Tian et al. 2018; 2016), especially when slow eye movements (Fig. 2) were significantly less effective in keeping the eye on target because of low gain. On the other hand, for very rapid oscillations (high frequencies), the oculomotor system was unable to keep track of the frequent flips in target position (even with saccades as opposed to smooth pursuit), and saccades were therefore more or less random events. Consistent with this, catch-up saccade amplitudes (Fig. 4B) were always small for all frequencies <1 Hz; on the other hand, catch-up saccade amplitudes increased for higher frequencies.

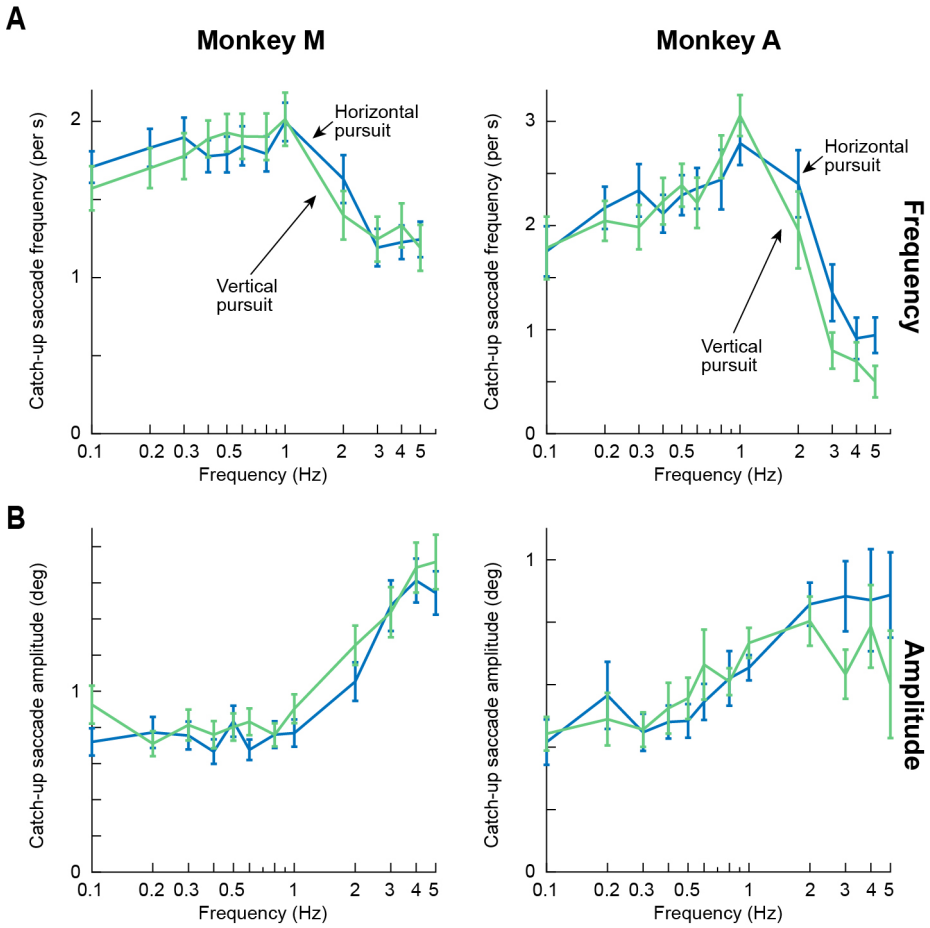

Figure 4 Catch-up saccade frequency was highest for frequencies resulting in maximal smooth velocity gain; catch-up saccade amplitude increased for high frequencies. (**A**) For both animals in Experiment 1, we estimated the frequency of catch-up saccades during steady-state smooth pursuit. The highest rate of catch-up saccades occurred at the frequencies associated with maximal smooth velocity gain (Figs. 1-3). For yet higher frequencies, both animals showed a marked decrease in catch-up saccade frequency, suggesting that the reduction in smooth velocity gain associated with these frequencies (Figs. 1-3) was not compensated for by rapid back and forth saccades to try to track the target. (**B**) Instead, catch-up saccades at higher frequencies were apparently random, infrequent movements that were increasingly large in amplitude. These patterns of results (**A** and **B**) were identical for horizontal and vertical pursuit, despite the quantitative difference in smooth velocity gain for these different pursuit directions (Figs. 2-3). All error bars denote 95% confidence intervals.

The above interpretations are also supported by inspecting sample eye position traces from two example temporal frequencies from Experiment 1 (Fig. 5). Saccades were

frequent at low temporal frequencies, and they kept the eye hovering around target location, consistent with the role of fixational microsaccades in continuously optimizing eye position (Guerrasio et al. 2010; Ko et al. 2010; Tian et al. 2018; 2016). On the other hand, saccades at high temporal frequency were less frequent, large, and very often increasing eye position error, rather than decreasing it, for substantial amounts of time (>500 ms).

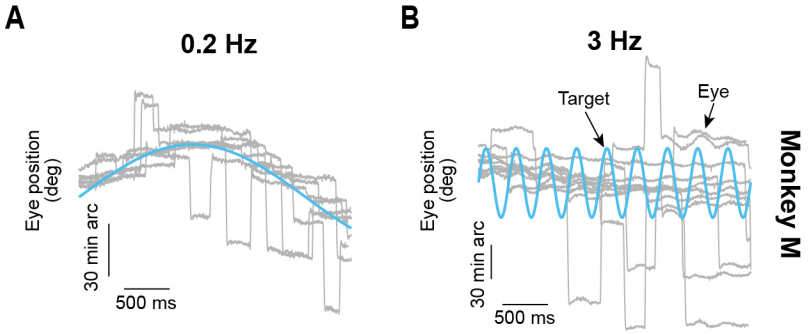

Figure 5 Monkey catch-up saccades at low temporal frequencies behaved like microsaccades during fixation. (**A**) Example eye position traces (gray) when tracking a target moving at 0.2 Hz (true target position is shown by the blue sinusoid). Smooth velocity (i.e. slow ocular drifts) tracked target motion, albeit at a low gain, and there were plenty of catch-up saccades. Thus, the slow eye movements here appeared similar to fixational ocular drifts in terms of velocity (e.g. inset in Fig. 3A). Moreover, catch-up saccades were quite frequent, and resulted in the eye "hovering" around target position on average, as with fixational microsaccades. (**B**) At high frequencies, slow movements also tracked the target motion (at low gain). However, this time, catch-up saccades were less frequent, and they were large, often deviating the eye substantially away from the target, and for substantial periods of time (>500 ms).

It is also interesting to note that despite the large difference in smooth pursuit gain between horizontal and vertical tracking in Experiment 1 (Fig. 2), catch-up saccade frequency and amplitude were not at all different from each other across tracking directions (Fig. 4). This might suggest that there is a larger tolerance for oculomotor

errors along the vertical dimension, perhaps because of potential asymmetries in oculomotor circuits (Hafed and Chen 2016), although this remains to be just a hypothesis at the moment.

Over-tracking of oblique small-amplitude slow motion trajectories by monkeys

We also sought to compare the effects of temporal frequency that we observed above to those of movement amplitude and direction for a given frequency. We therefore conducted Experiment 2 (Materials and Methods) in which temporal frequency was pegged at 0.5 Hz but movement amplitude varied between ~15 min arc (0.25 deg) and ~2 deg (Materials and Methods). Movement direction also included oblique tracking (Materials and Methods). Overall, we found expected results in terms of smooth pursuit gain as a function of target motion trajectory amplitude. For example, for both cardinal (horizontal and vertical) and oblique pursuit, smooth pursuit gain increased with increasing target motion amplitude (Fig. 6). This might explain why our results from Experiment 1 above showed band-pass behavior (Fig. 2) when the target amplitude was small; this band-pass effect was primarily due to the very small motion trajectory amplitudes (and, correspondingly, velocities) used when compared to classic studies, and increasing amplitude in the current experiment has alleviated this.

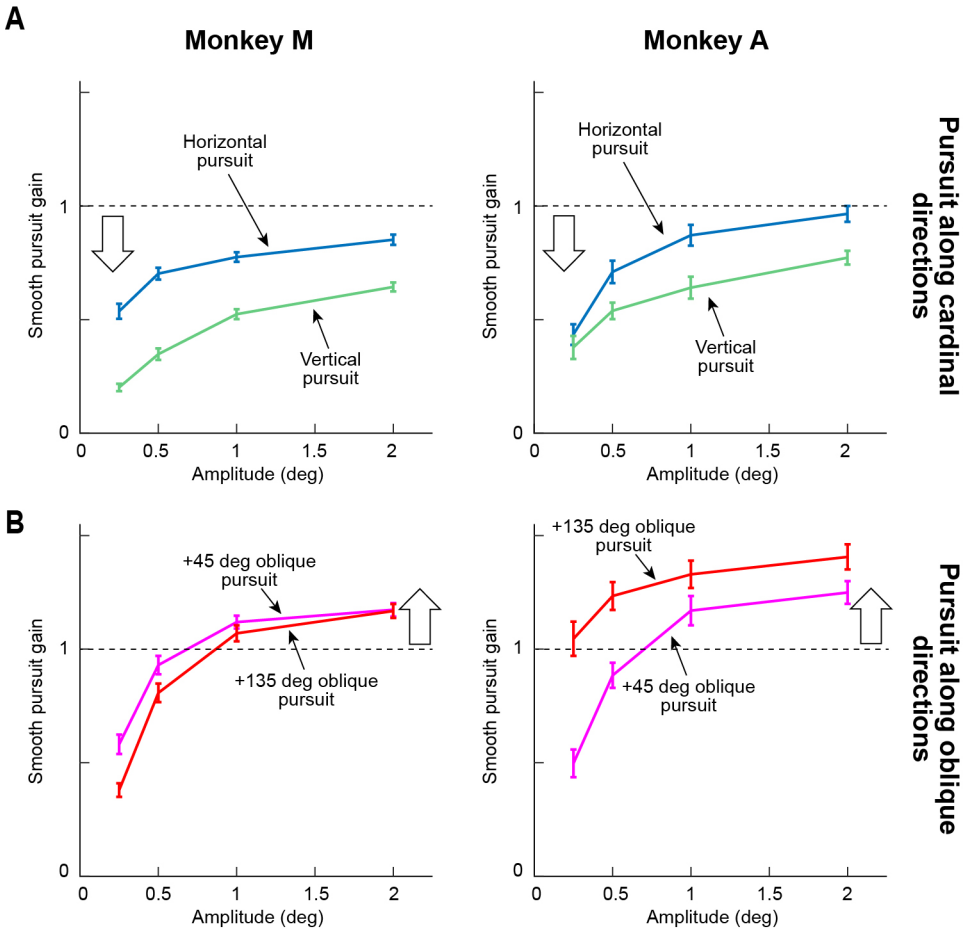

Figure 6 Higher pursuit gain for tracking of small-amplitude oblique motion trajectories. (**A**) In Experiment 2, we varied target sinusoidal position amplitude, and also introduced oblique pursuit trajectories. For cardinal directions, we obtained expected results based on what we found in Experiment 1. Pursuit gain was higher for horizontal than vertical pursuit, and pursuit gain progressively increased with increasing target amplitude. Note, however, that gain seemed to asymptote near a value of 1. (**B**) For oblique pursuit directions, there was still an increase in pursuit gain with target amplitude. However, this increase eventually resulted in an overshoot of target speeds (gain going substantially >1). Even at 0.5 deg amplitudes, oblique pursuit showed higher gain than cardinal pursuit (compare the 0.5 deg point in this panel to the corresponding point in panel **A**). Thus, oblique pursuit was associated with overshooting of target velocity in both animals. All error bars denote 95% confidence intervals.

The most striking result from Experiment 2, which is also evident in Fig. 6, was that smooth pursuit gain was significantly >1 for oblique tracking directions (Fig. 6B). This is different from pursuit of large-amplitude motions, in which oblique pursuit might be

expected to be worse in gain than pursuit along cardinal directions, perhaps due to oblique effects in motion perception (Krukowski and Stone 2005). When we analyzed the horizontal and vertical components of oblique pursuit independently, we found that the "overshoot" was primarily occurring in the horizontal dimension (Fig. 7). These results are reminiscent of overshoot in visually-guided saccade amplitudes in humans for very small retinal eccentricities (Kalesnykas and Hallett 1994), and they demonstrate an additional difference in the control capabilities of the slow movement oculomotor sub-system between small and large motion amplitudes. For example, in large-amplitude pursuit, horizontal gain can be higher than vertical gain during oblique tracking (Rottach et al. 1996), but overall gain still always stays below or very close to 1. We found marked increases above a gain value of 1.

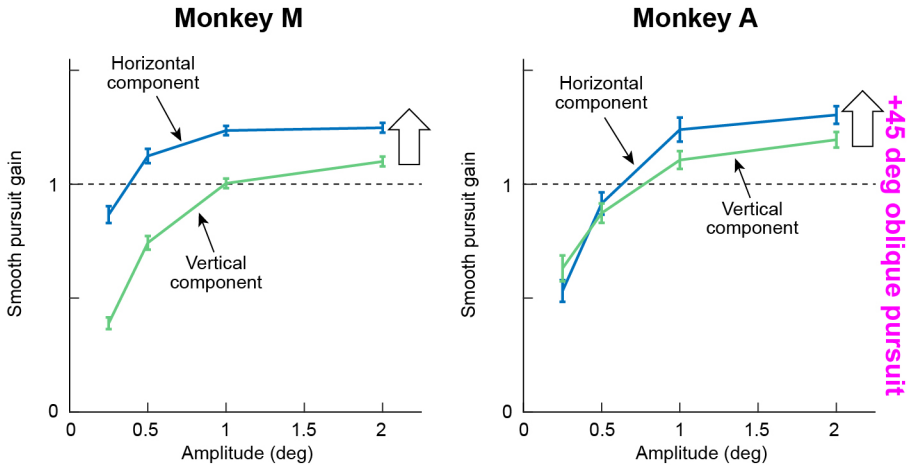

Figure 7 Over-tracking in the horizontal dimension during smooth pursuit of small-amplitude oblique motion trajectories. We investigated the overshoot observed in Fig. 6B by plotting the horizontal and vertical components of eye velocity separately for an example oblique pursuit condition. In both animals, pursuit gain was higher in the horizontal component of eye velocity than the vertical component. Thus, the over-tracking observed in Fig. 6B was primarily driven by over-tracking in the horizontal dimension. All error bars denote 95% confidence intervals.

The over-tracking of oblique motion trajectories was also accompanied by larger catch-up saccades for these trajectories. In Fig. 8, we plotted catch-up saccade frequency (Fig. 8A) and amplitude (Fig. 8B), as we had done earlier for Experiment 1. Consistent with Experiment 1, increased smooth pursuit gain was associated with an increase in catch-up saccade frequency (Fig. 8A), suggesting synergistic interactions between smooth pursuit eye movements and saccades to optimize eye position on the target (de Brouwer et al. 2002); this is similar to us seeing the most catch-up saccades in Experiment 1 for the temporal frequencies in which smooth velocity gain was also at a maximum. In terms of catch-up saccade amplitude, it also increased with increasing target motion amplitude; in addition, while an increase in saccade amplitude was expected with increasing target position trajectory amplitude, the increase was stronger for oblique directions (Fig. 8B). For example, in monkey A, both oblique directions had higher saccade amplitudes than horizontal or vertical trajectories, and in monkey M, one of the oblique directions did. This result might reflect the slightly higher peak velocities associated with oblique tracking (for example, oblique tracking with a horizontal and vertical amplitude of 2 deg each meant an overall radial amplitude of 2.82 deg; Materials and Methods).

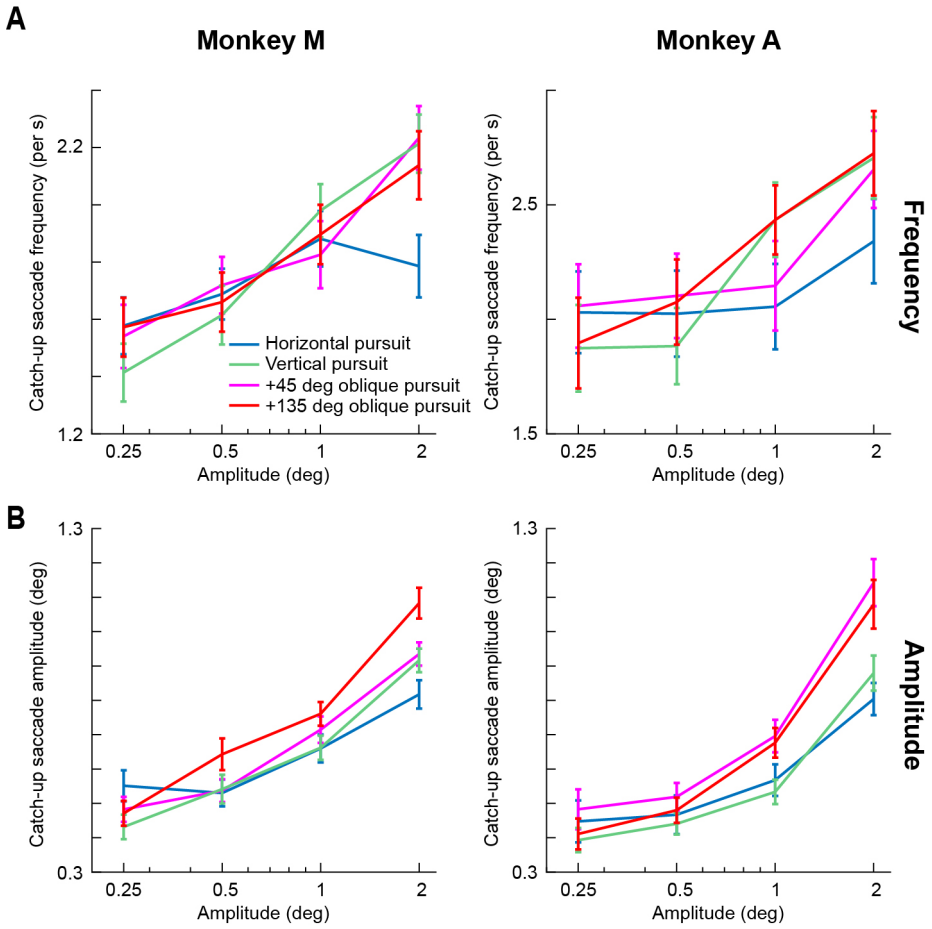

Figure 8 Catch-up saccade frequency and amplitude in Experiment 2. (**A**) Consistent with Experiment 1, when smooth velocity gain was high (Figs. 6-7), catch-up saccade frequency was high. (**B**) Catch-up saccade amplitude also expectedly increased with larger target motion excursions. All error bars denote 95% confidence intervals.

Dependence of monkey first catch-up saccade latency and smooth pursuit initiation on target motion

We also analyzed the properties of the very first catch-up saccade during smooth pursuit initiation, as well as the smooth component of initial eye acceleration itself. For all saccades (including fixational microsaccades) occurring in the interval 0-300 ms after target motion onset, we plotted these movements' amplitudes as a function of their occurrence time. We also plotted either baseline eye velocity (in the 50 ms interval

598 starting at -100 ms from target motion onset) or smooth pursuit initiation eye velocity (in
599 the 50 ms starting 100 ms after target motion onset; ensuring no saccades within each
600 interval). We observed expected relationships between initial catch-up saccades and
601 initial smooth pursuit eye velocity. For example, in Experiment 2, with 0.5 Hz target
602 trajectory variation, eye position error of the target (relative to initial fixation location if
603 the eye did not start tracking) monotonically increased in the first 300 ms of any trial (and
604 up to 500 ms). Therefore, if a saccade were to occur during initiation (and there was no
605 associated smooth acceleration after motion onset), then saccade amplitude was expected
606 to increase with increasing time after motion onset. However, this was not the case for
607 most target amplitudes that we tested (Fig. 9A). We think that this is so because of a
608 concomitant increase in smooth eye velocity to track the target (Fig. 9A, B; only
609 horizontal tracking data is shown for clarity). In other words, after motion onset, the eye
610 often started to accelerate smoothly, therefore already reducing eye position error. Such
611 reduction may have alleviated the need to increase first catch-up saccade amplitude. Only
612 when target position amplitude was large enough (2 deg) did there arise a need for
613 increasing initial catch-up saccade amplitude. For such a larger position amplitude of the
614 motion trajectory, even the initial component of smooth pursuit acceleration was not
615 sufficient to reduce eye position error sufficiently; a larger saccade was therefore
616 necessary. This idea is illustrated in Fig. 9C showing raw pursuit velocities with saccades
617 excised from the averages as per Materials and Methods (shown from horizontal tracking
618 only for clarity). Pursuit initiation velocity increased for trajectories with amplitudes of 2
619 deg compared to, say, 0.5 deg. However, the increase in velocity did not necessarily
620 allow for completely eliminating eye position error, resulting in the need for an initial

catch-up saccade whose amplitude gradually increased with increasing time after motion onset (Fig. 9A; 2 deg motion position amplitude). Therefore, there was a synergistic interaction between smooth pursuit initiation and initial catch-up saccade execution, which also likely occurs between slow ocular drifts and microsaccades (Chen and Hafed 2013). Note that in Fig. 9A, saccades occurring <50-60 ms after target motion onset were fixational microsaccades and not really target-driven catch-up saccades because they occurred too early to reflect the new visual error signal introduced by target motion onset. This is why these movements were also small in amplitude even for 2 deg motion amplitudes.

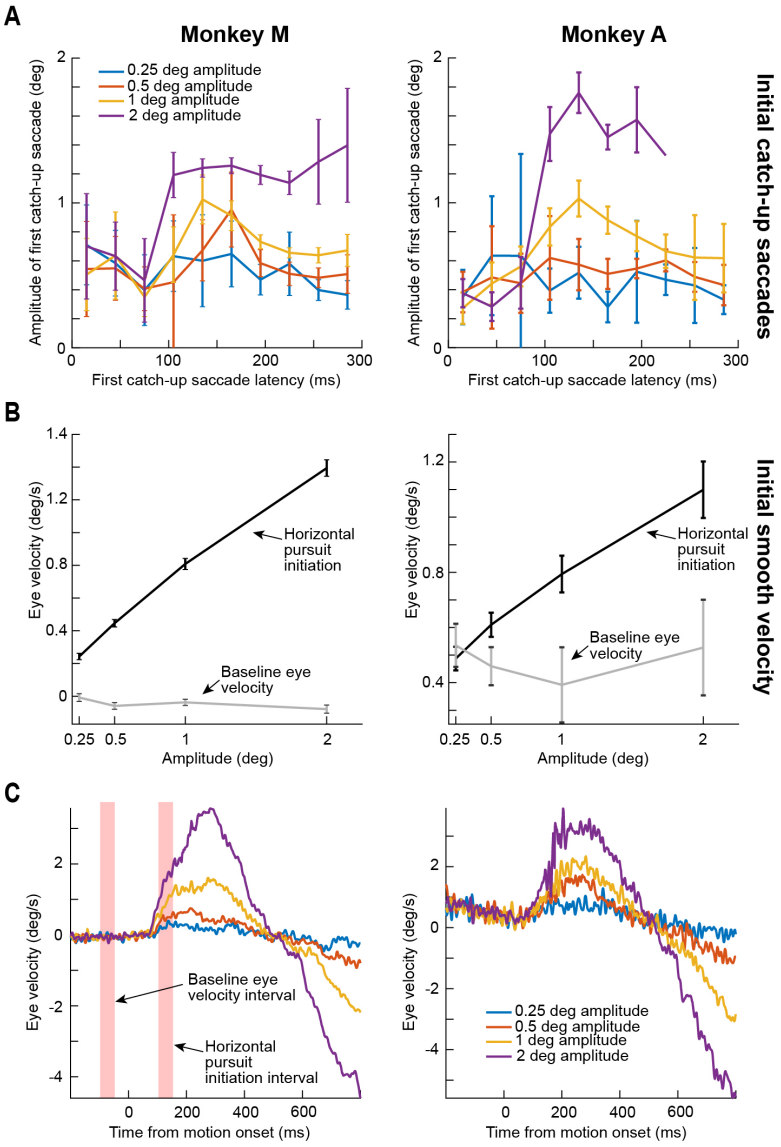

Figure 9 Interactions between saccades and smooth pursuit eye movements during initiation of tracking. (**A**) We found evidence of synergistic interactions between smooth pursuit and catch-up saccades during initiation. The amplitude of the first catch-up saccade after target motion onset did not increase convincingly as a function of time (even though eye position error was monotonically increasing), except for 2 deg amplitude trajectories (dark purple). (**B**) This might be because saccade-free smooth pursuit initiation may have already acted to reduce eye position error. For example, initial eye velocity during saccade-free initiation (see pink measurement intervals in the left panel of **C**) increased with increasing target amplitude. Thus, saccades did not necessarily need to increase in amplitude in **A** for small target amplitudes. For 2 deg trajectories, the increase in smooth eye velocity may have not been sufficient to completely obviate the need for a catch-up saccade, and that is why catch-up saccade amplitudes in this particular condition increased with time from motion onset when compared to all of the other conditions that we tested. Note that in **A**, saccades with latencies less than ~50-60 ms were likely not initial catch-up saccades but instead fixational microsaccades. That is why their amplitudes were low for all conditions. (**C**) Example average saccade-free smooth velocity traces from horizontal tracking (like **B**) showing the measurement intervals for **B** and also the idea that smooth velocity effects increased with increasing target amplitude. All error bars denote 95% confidence intervals.

Finally, we checked whether the first catch-up saccade latency itself depended on target amplitude. In Experiment 2, we plotted histograms of first catch-up saccade latency in the different amplitude conditions (Fig. 10). For the smallest amplitude trajectories, catch-up saccade latencies were long and variable. As target amplitude increased, latency became more precise, as well as shorter. Since Fig. 9 showed that it was more likely for catch-up saccade amplitudes to increase with increasing target position amplitude, these results constitute a monkey replication of human studies, showing that saccade latencies are substantially longer for very small-amplitude visually-guided saccades compared to larger ones (Kalesnykas and Hallett 1994).

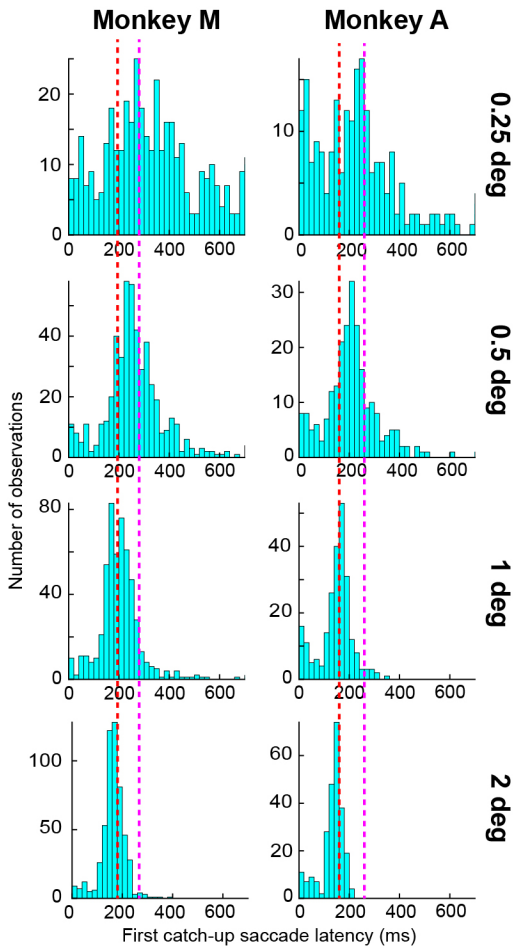

Figure 10 Dependence of first catch-up saccade latency on target amplitude. We plotted histograms of first catch-up saccade latency for different target amplitudes in Experiment 2. We show results only from horizontal tracking for clarity; other directions showed similar effects. Since larger target amplitudes resulted in larger catch-up saccades (e.g. Fig. 9), the present histograms show monkey replication of human observations that very small visually-guided saccades are associated with longer reaction times than larger ones (Kalesnykas and Hallett 1994). For example, for each monkey, the red dashed line marks the latency bin with most observations at 2 deg target motion amplitude (bottom panel), and the magenta dashed line marks the latency bin with the most observations at 0.25 deg target motion amplitude (top panel). As can be seen, there was a substantial differential in saccade times for the different target motion amplitudes. Note that, like in Fig. 9, the small distribution of saccades occurring with latencies <100 ms in this figure are likely not genuine first catch-up saccades, but instead fixational microsaccades. This is further supported by the noticeable dip in the histograms at ~100 ms, which is similar to the phenomenon of microsaccadic inhibition reported in the literature for both humans and monkeys (Buonocore et al. 2017; Hafed and Ignashchenkova 2013; Rolfs et al. 2008).

682 **Discussion**

683

684 We attempted to characterize monkey oculomotor behavior with small-amplitude slow
685 motion trajectories. We catalogued both smooth velocity effects as well as catch-up
686 saccade effects. For smooth velocity effects, we found that pursuit gain was low for both
687 low and high temporal frequencies, only reaching a peak in mid-frequencies near 1 Hz.
688 This is in contrast to previous human experiments with large-amplitude (Collewijn and
689 Tamminga 1984; Fabisch et al. 2009; Rottach et al. 1996) or small-amplitude (Martins et
690 al. 1985) sinusoidal motions, in which low-pass behavior was observed. In terms of
691 catch-up saccades, we found that they (perhaps paradoxically) increased in frequency
692 when smooth velocity gain was high. Moreover, we found that catch-up saccades during
693 presentation of low temporal frequencies acted more like fixational microsaccades,
694 whereas catch-up saccades during presentation of high temporal frequencies were large
695 and infrequent.

696

697 Our results provide a necessary foundation for exploring the neural mechanisms
698 subserving fixational ocular drifts in awake monkeys. This complements early
699 characterizations of awake monkey smooth pursuit eye movements with higher speeds
700 (Lisberger and Westbrook 1985). These early characterizations were themselves a major
701 boon for a wide range of significant and seminal subsequent discoveries about the neural
702 mechanisms for oculomotor control in general, and about the neural mechanisms for
703 smooth pursuit in particular (Krauzlis 2004). Our next goal is to extend on our current
704 results by uncovering neural substrates in the same animals.

To that end, we were careful to avoid unnecessarily penalizing the monkeys for making saccades during tracking. Specifically, we aimed to minimize over-training on one particular movement modality. For example, early human studies with small-amplitude motions barely had any saccades in the experiments, to focus almost solely on slow control effects (Martins et al. 1985). However, we wanted the animals to engage in as naturalistic a behavior as possible, such that we could understand important interactions between slow control and micro/saccadic control. This has allowed us to make the interesting observation that smooth pursuit gain in our monkeys exhibited band-pass behavior, unlike in (Martins et al. 1985). This has also allowed us to make the interesting observation that there were actually more saccades when pursuit gain was high (i.e. when retinal position and motion errors were presumably low) than when it was low.

Such an observation of a concomitant increase in catch-up saccade frequency along with an increased velocity gain might suggest that catch-up saccades normally behave like fixational microsaccades. The latter eye movements continuously re-align gaze with a foveal target under a variety of stimulus conditions (Guerrasio et al. 2010; Ko et al. 2010), and even when competing peripheral stimuli are presented (Tian et al. 2018; 2016). Their frequency of occurrence might therefore increase when the target is sharp, providing a clear spatial reference frame for re-aligning gaze. During pursuit, similar re-alignment of gaze may be necessary. This is consistent with observations that foveal targets increase catch-up saccade frequency in humans (Heinen et al. 2018; Heinen et al. 2016); presumably, foveal targets not only support good smooth velocity gain, but they

also provide the oculomotor system with a punctate spatial reference point to which gaze can be re-directed. We also found in monkeys that there was a tendency for higher catch-up saccade frequencies for smaller foveal pursuit targets than for bigger and fuzzier ones (Hafed et al. 2008). It would be interesting to analyze the relationship between eye position error and catch-up saccade likelihood with a foveal target during smooth pursuit, such that one can uncover an almost-deterministic estimate of whether a catch-up saccade can occur at any one moment of time or not (de Brouwer et al. 2002). This kind of approach was recently made for microsaccades (Tian et al. 2018), and it is very intriguing because predicting whether and when a microsaccade might take place can then, at least in principle, be used to estimate the occurrence of distinct cognitive performance effects associated with such movements (Bellet et al. 2017; Chen et al. 2015; Hafed 2013).

Our interest in relying on more naturalistic tracking (i.e. with combined smooth and saccadic eye movements) may also explain why we observed band-pass smooth pursuit gain effects in our monkeys, even though a similar human experiment with low frequencies and small-amplitude trajectories found very good gain (Martins et al. 1985). As stated earlier, in that study, the human subjects tested were highly trained, and they were instructed to minimize saccade generation. As a result, substantial systematic eye position drifts occurred in their experiments, whereas we did not observe such systematic drifts. In our case, we relied more on the natural behavior of the monkeys in being intrinsically interested to foveate the small white spot that was presented on the display. Yes, the monkeys became highly trained in the lab after multiple sessions, but their behavior was not shaped by us, say, by aborting trials whenever a saccade occurred.

Instead, we rewarded them for tracking the target to within a reasonable radius, which may not be too different from natural variability in human fixation among untrained individuals (Cherici et al. 2012). As a result, our monkeys tracked the target with both smooth and saccadic eye movements.

We were also intrigued by our oblique tracking effects in Experiment 2. Both smooth velocity gain and catch-up saccade amplitudes increased for oblique tracking, with smooth velocity gain surpassing a value of 1 by quite a margin. While the catch-up saccade amplitude increase may have reflected the slightly faster trajectories associated with oblique target motions in our stimulus design relative to cardinal target motions (Materials and Methods), the smooth velocity gain measure is a normalized measure that should not depend on absolute target velocity. Instead, it does reflect a real observation that pursuit in these oblique conditions substantially over-tracked the small-amplitude motions that we tested. This is intriguing to us because small visually-guided saccades in humans are known to overshoot their targets (Kalesnykas and Hallett 1994). We may have thus observed a similar phenomenon for smooth pursuit, adding to evidence that pursuit and saccades share neural resources (Krauzlis and Dill 2002; Krauzlis 2004; Krauzlis et al. 1997; Krauzlis et al. 2017). Similarly, even our catch-up saccade effects of Fig. 10 demonstrate a monkey correlate of human observations that visually-guided saccade latency increases for small target eccentricities. It would be interesting to extend these effects for other types of saccades, like delayed visually- or memory-guided saccades.

In all, our results add to an extensive cataloguing in the literature of rhesus macaque sensory, perceptual, cognitive, and motor capabilities, testifying to the tremendous value of such an animal model for systems neuroscience research.

Acknowledgments

We were funded by the Werner Reichardt Centre for Integrative Neuroscience (CIN) at the Eberhard Karls University of Tübingen. The CIN is an Excellence Cluster funded by the Deutsche Forschungsgemeinschaft (DFG) within the framework of the Excellence Initiative (EXC 307). We were also funded by the DFG through a Research Unit (FOR 1847). ZMH was additionally funded by the Hertie Institute for Clinical Brain Research at the Eberhard Karls University of Tübingen.

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