Visual Fixation Handout

Purpose of Fixation Control:

Velocity and position errors must be kept to a minimum to optimize acuity for stationary objects. At the same time, some movement must occur or else the image fades completely.

Measurement of Fixation:

Much of the activity involved in fixation involves movements on the scale of a few arcmin, so a high resolution eye tracker is required to see them, such as a search coil or dual Purkinje image tracker.

Dynamics of Visual Fixation**:**

The eye is always moving, and the natural motion of the eye during fixation is sometimes called **Physiological Nystagmus**. It involves three components:

High frequency tremor of the eyes occurs at a rate of 50 to 100 Hz! The movements are about half an arc minute in amplitude and are uncorrelated in the two eyes. They may be the result of individual spike discharges in motor neurons.

Slow Drift movements occur as well, sometimes generating errors and sometimes correcting them. They may be conjugate or disconjugate.

MicroSaccades occur about 3 times per second with an amplitude of about 6 arc minutes (0.1 degree) and are visible during ophthalmoscopy, but are hard to see with direct observation. These tend to be conjugate. MicroSaccades can be suppressed with concentration. Fixation MicroSaccades fall on the *Main Sequence* for saccadic eye movements, which relates velocity to amplitude, indicating that they are typical, though tiny, saccades.

Fixation System or Pursuit at zero velocity (slow control system)?

Visual fixation has been suggested to be no more than pursuit of a target at zero velocity. We can fixate just using slow movements without saccades. While pursuit may play a role in reducing drift, several lines of evidence suggest that Visual Fixation is an Oculomotor Control System unto itself:

No Oscillations: Small oscillations which accompany pursuit are absent with fixation

Clinically separate: Some patients have steady fixation, but break into nystagmus when they try to pursue.

Fixation Cells: Certain Parietal Lobe neurons fire during fixation but not during pursuit.

Saccade inhibition: During fixation, saccades are harder to evoke by stimulating cortical cells, compared to during pursuit.

No effect of MST stimulation: During Pursuit, stimulation of MST changes the velocity of the eye movement, but during fixation there is no pursuit generated.

Disorders of Fixation control

Fixation is disrupted whenever inappropriate eye movements occur on attempted steady gaze. These can be **square wave jerks** (back to back saccades in opposite directions) which occur occasionally in normals, more often under fatigue, and still more often when saccades are insufficiently inhibited. Another example is **congenital nystagmus**, in which the eye drifts away from the desired fixation point and must be reset with a saccade.

Eccentric Fixation occurs when patients have a central scotoma, such as occurs for example with Age Related Maculopathy . Typically such patients will pick a particular spot outside their fovea to fixate with, although ARM patients tend to me more variable than young patients with central scotomas. Strabismics with amblyopia will also sometimes show eccentric fixation, even though their fovea may be intact.

NEURAL CONTROL OF GAZE CHANGING

Whereas VOR, OKN and Pursuit movements all have the function of stablizing the world, or a particular object image, the saccadic system serves to change our gaze from one point to another.

Saccadic System:

Pupose of Saccades:

- To alter gaze from one object of interest to another under effort of will (voluntary saccades): Ex. Reading; searching for a face in a crowd. Scan Paths
- To alter gaze to a sudden event in the periphery (reflex saccades): Ex. Orienting to a sudden noise or flash
- To reset gaze after VOR or OKN has carried it to an extreme (Fast phases of Nystagmus)
- To correct small errors of fixation (fixational microsaccades).
- To correct small errors in pursuit (catch-up or back-up saccades.)

Measurement of Saccades:

Saccades are easy to detect, and are easily visible even under direct observation because the eye moves so quickly. Accurate measurement of saccade dynamics requires a sophisticated system because the saccades are so fast, and a search coil is best. The Dual-Purkinje image system, although very sensitive, has a lens wobble artifact which obscures the true dynamics of the saccade. Because of lens wobble, there is about 1/2 degree difference between globe position and retinal image position at the end of a 12 degree saccade. This error lasts only about 10-20 msec. Video trackers sample too infrequently to capture the dynamics of saccades.

Vision During Saccades:

Many studies have shown that vision is disrupted during saccades, a phenomenon called **Saccadic Omission.** Saccadic Omission occurs because of

Visual Masking in which the image seen before (foreward masking) and after (backward masking) the saccade tend to mask the image seen during the saccade.

Retinal Blur, which describes the loss of contrast in images as they move rapidly across the retina because the retina has limited temporal resolution.

Saccadic Suppression, in which some central mechanism disrupts visual processing during saccades. A better name is Saccade Related Visual Suppression because it is visual sensitivity that is suppressed. Visual Suppression also accompanies eye blinks, but not smooth pursuits.

Retinal Shearing has also been proposed, but never demonstrated, in which the dramatic forces involved in saccades may disrupt processing in the retina.

Dynamics of Saccades:

Saccades are probably the most heavily studied of all the eye movements because they are so dramatic and involve a complex control system. The basic characteristic of all saccades is that the eye moves as fast as it possibly can from one point to another, at the expense of vision during the eye movement.

Yoking:

Saccades are conjugate eye movements, only in very rare neurological conditions do you see oppositely-directed saccades. This yoking is accomplished at the level of the abducens nucleus interneurons. In horizontal saccades, there is transient divergence because the abducting eye tends to go faster and farther than the adducting eye. Remaining divergence is corrected at the end of the saccade by a slow drift. In vertical saccades there is a transient horizontal divergence with upward saccades and a horizontal convergence with downward saccades.

Latency:

Saccades have a latency of typically about 200 msec. This is significantly longer than OKN, pursuits or vergence, and more than ten times longer than VOR. Many factors influence saccade latency: longer latencies occur with weak (dim or low contrast) targets, unpredictable targets, and with older subjects. Shorter latencies occur with brighter targets, predictable targets, with auditory stimuli, and with younger subjects. Timing of fixation target and saccade target make a big difference (Gap vs. Overlap tasks). So-called "**Express Saccades**" with latency as low as 100 msec occur under certain special conditions, when a fixation target is

extinguished 200 msec before the saccade target comes on and when the possible locations of the saccade target are limited or highly predictable. This may be related to how fast we can shift attention, and/or it may reflect the action of the fixation system.

Velocity:

Saccades have a very high velocity, up to 800 or even 1000 degrees per second for very large saccades. Saccade velocities follow a very specific, predictable pattern such that the peak velocity of the saccade is dependent on its amplitude. This has been called **the Main Sequence** for saccades, borrowing a term from Astronomy. There is also a tight relationship between Duration, Velocity and Amplitude, also referred to as a Main Sequence. Large saccades last longer and have higher velocities than small saccades. Normal saccades will always fall near this Main Sequence, and if they don't it may indicate neurological or neuromuscular disfunction. Saccades associated with fixation, OKN, VOR and **voluntary nystagmus** all fall on this Main Sequence.

A number of things affect saccade velocity to some degree: Velocities are lower with saccades away from primary gaze, with saccades made in the dark, saccades made in anticipation of target motion, saccades made to targets that are imagined or remembered. These variables can make about a 10% difference in velocity relative to the Main Sequence.

Programming of Saccades:

Unlike Pursuit movements, which are continuously controlled, saccades must be reprogrammed after each fixation period. In most cases, if a target moves during a saccade, the saccade in progress is not modified and the next saccade will not occur until one latency period after the end of the first saccade. For this reason, saccades have been called **Ballistic**, meaning that they are determined before they are "launched" and cannot be redirected during "flight." Other analogies include passing vs. dribbling in soccer or firing a projectile like a bullet vs. guiding a missle carying the space shuttle.

EXCEPT: Saccades can sometimes be modified during flight, and numerous experiments have shown that some subjects are able to incorporate visual information presented during a saccade to modify the ongoing saccade. For example, some subjects can make a curved saccade when presented with a target that steps right and then up.

BOTTOM LINE: Saccades are usually programmed one at a time and vision during saccades is poor, so these exceptions are probably mostly laboratory phenomena.

Pulse and Step components:

In order to achieve the extremely high velocities which occur during saccades, the innervation involves a very high **pulse** of activity initially, followed by a **step** change in firing. Without the pulse, the eye would just glide slowly to the new position because of viscosity. The pulse determines the velocity and amplitude of the saccade, while the step determines the final position of the eye. Current evidence suggests that the step is formed from the pulse by a process of neural integration, very much like the integration that occurs for VOR and pursuits. In recordings from motor neurons, one often sees a **Pulse-Slide-Step** sequence (the saccadic waltz) , where the slide is a gradual transition between the other two.

Saccade accuracy:

Normal saccades are usually either on target or a bit smaller than needed (hypometric). Innaccurate control of saccades is termed **saccade dysmetria** (*dys* -bad + *metria* - measure). Undershoots are termed **hypometric** and overshoots are termed **hypermetric**. When saccades undershoot, they may slide to the target in a movement called a **Glissade**. If the pulse component is wrong, the saccade will be dysmetric. If the pulse component is weak or absent, it results in **slow saccades**. If there is a **Pulse-Step mismatch**, the saccade will end on target but the eye will then drift away to a different point. If the step is formed by a **Leaky Integrator**, gaze will always slip back toward primary gaze, resulting in **gaze-evoked nystagmus**. End-point nystagmus is one example of this.

Pathway for Saccades

General considerations

The Saccadic control pathway involves a large number of areas in both cortex and brainstem. Some specialization of function can be identified for these areas with respect to the following:

- voluntary selection of saccade targets,
- reflex programming of saccades,
- inhibition of saccadic pulse generation (pause cells),
- saccadic pulse generation itself (burst cells), and the
- integration of the pulse to form the step component.

Production of pulse and step:

Within the last two decades, physiologists have found centers which appear to be responsible for the generation of pulse and step components in saccades, and an additional mechanism which coordinates all saccadic pulses. Pulse signals are formed by **Excitatory Burst Neurons** (**EBN**) which fire during the saccade. The frequency of firing determines the velocity of the saccade and the duration of firing determines the amplitude of the saccade. Normally, these quantities are closely related

(the Main Sequence). In addition, there are **Inhibitory Burst Neurons (IBN)** which fire during the saccade and serve to shut down the antagonist muscle.

The Step is formed by **Neural Integrators** which receive the pulse signals and add them up over time**.**

All of the Burst Neurons are inhibited by **Pause Neurons**, which fire continuously except during saccades. One important role of the Pause Neurons is to keep all of the Burst Neurons coordinated, so that they all fire at once for the maximum possible velocity of eye movement. They also control the duration of the pulse which greatly aids the stability of the movement.

Brainstem:

Final Common Path: Just as the Cranial Nerve Nuclei form the final common path for all eye movements, supranuclear saccadic control centers form the final common path for all rapid eye movements, such as fast phases of nystagmus, fixational microsaccades, voluntary and reflex saccades. These control mechanisms give rise to the characteristic Main Sequence behavior of all saccadic eye movements.

PPRF (Paramedian Pontine Reticular Formation): located at the level of the Abducens Nucleus, it contains Burst Neurons which form the pulse component of horizontal saccades. It receives inputs from the contralateral Superior Colliculus and Frontal Eye Fields. It projects directly to the ipsilateral Abducens nucleus and also to the Neural Integrators in the Nucleus Prepositus Hypoglossi. Stimulation of the PPRF produces saccades to the same side.

riMLF (rostral insterstitial nucleus of the MLF) also called the MRF (Mesencephalic Reticular Formation): located rostral to the Oculomotor Nucleus , it contains Burst Neurons which form the pulse component of both vertical and torsional saccades. Its inputs are similar to the PPRF. It projects to the ipsilateral Oculomotor and Trochlear Nuclei, and also to Neural Integrators in the interstitial nucleus of Cajal.

The riMLF organization is best understood in terms of fast phases of VOR. Fast phases for the Right Anterior and Posterior canals are generated through the Right riMLF to the Right Oculomotor Nucleus and Trochlear Nucleus. Fast phase for Right Anterior Canal involves primarily the Right IR and Left SO muscles, which depress and dextro-tort the eyes. Fast phase for Right Posterior Canal involves primarily the Right IO and Left SR muscles, which elevate and dextro-tort the eyes. Notice that the Right riMLF can either elevate or depress, but always dextro-torts.

So, stimulation of the riMLF on one side produces ipsilateral extorsion, contralateral intorsion, and either upward or downward saccades. Thus

loss of the riMLF on one side has a big effect on torsion but doesn't abolish either direction of vertical movement. Bilateral loss of the riMLF abolishes vertical saccades.

Nucleus Prepositus Hypoglossi: presumed site of the neural integration which converts signals from burst neurons into tonic position signals for horizontal saccades. Thus, it contributes the step component of the saccadic control signal.

Interstitial Nucleus of Cajal: presumed site of neural integration for vertical and torsional saccades, contributing step component for these directions.

Nucleus Raphe Interpositus: located on the midline, between the rootlets of the Abducens Nerves. This area contains Pause Neurons which fire continuously except during saccades. These Pause Neurons inhibit Burst Neurons for all directions of saccades, and so play an important role in fixation and in saccade timing.

Cerebellum:

As for other types of eye movements, saccades are modified through the action of the Cerebellum, allowing for adjustment of saccade amplitude based on visual feedback. The Dorsal Vermis and the Fastigial Nucleus of the Cerebellum are both implicated in saccade pulse modulation, and there are projections both contralaterally and ipsilaterally to the PPRF and riMLF. Removal of these structures leads to saccade dysmetria. Velocities and latencies are normal, but amplitudes are typically too large. This suggests that the normal function of the Cerebellum is to tone down the size of saccades to keep them accurate. In an extreme case, one may see macrosaccadic oscillations, in which the eye makes continual saccades back and forth across a target, always overshooting and then trying to correct.

The Flocculus appears to play a similar role in adjusting the size of the step component to match the pulse. Focal lesions of the Flocculus lead to postsaccadic drift because of the resulting Pulse-Step mismatch.

Superior Colliculus

Dorsal layers: has visual sensitivity with a map of retinotopic space; also has auditory map which shifts with eye movements, so that the auditory map and visual map stay registered!

Ventral layers: has motor map which codes the direction of the next saccade to be made. Stimulation of SC on one side produces a horizontal saccade toward the opposite side.

Caudal Pole of SC encodes large horizontal saccades to opposite side, moving rostrally one finds stimulation produces smaller and smaller saccades, and the Rostral Pole encodes fixation. Medial half of SC

encodes upward saccades, Lateral half encodes downward saccades. Bilateral stimulation is required for purely vertical saccades.

Basal Ganglia:

The Caudate Nucleus and the Substantia Nigra both play a role in controlling the Superior Colliculus so that reflex saccades do not occur inappropriately.

Cortical areas involved in saccades:

Stimulation of these areas produces a saccade toward the opposite side, which may include an upward or downward component. Bilateral stimulation is required for purely vertical saccade.

V1 (Striate Cortex): sends signals directly to the ipsilateral Superior Colliculus, as well as to other cortical areas.

FEF (Frontal Eye Fields): sends signals to the ipsilateral Superior Colliculus; also projects to the contralateral brainstem areas where bursts are generated, the PPRF (for horizontal saccades) and riMLF (for vertical saccades). There is a rough retinotopic map in the FEF, and bilateral stimulation is required for a purely vertical saccade.

LIP: Lateral Inferior Parietal: Cells here project to the Superior Colliculus and to the FEF. The LIP seems to play a role in attention, just as the Posterior Parietal area does in Smooth Pursuit.

Disorders of Saccadic Eye Movements

Velocity Disorders

These are conditions which affect the rate at which the eye moves, which may or may not affect the accuracy of the saccade.

Saccades can be too fast in some situations, meaning that their velocity is higher than the Main Sequence would predict for their amplitude. A better way to think of these is that they are actually too small. **Myasthenia Gravis** is a disorder affecting the neuro-muscular junction and leads to rapid fatigue. Myasthenia patients often show their first signs in eye movements. They will start to make a large saccade and the eye will accelerate to an appropriate, high velocity, but then they suffer intrasaccadic fatigue and the eye stops short. So, you get very rapid, but very small saccades.

Restrictions in the orbit such as a tumor, might prevent the globe from rotating and stop a saccade before it reaches its target.

Saccades can be too slow in many situations. Usually it is because of a **peripheral loss of function**, such as an ocular muscle paresis or ocular motor nerve paresis. In this case, there will be a restriction in the range of eye movements as well as a slowing of saccades into the active field of the affected muscle or muscles.

A central neurological disorder is usually indicated when the range of eye movement is normal but saccades are slow. The most obvious candidate is the Burst Cells, because their firing rate determines the saccade velocity. If some of the burst cells are damaged then the remaining ones will have to fire for a longer time to get the same size saccade, resulting in a low velocity saccade. Their might also be a problem with the Pause Cells, however, because if they don't stop inhibiting some of the Burst Cells, it will mimic a loss of Burst Cells. By this logic, the problem could be farther up in the control pathway as well, if the Pause Cells are getting inadequate signals.

Accuracy Disorders

These are conditions which affect the size of the saccade relative to the target displacement. Errors can either be in the direction of the saccade or in the amplitude, with the latter being the most common.

Cerebellar Disfunction causes saccades to be inaccurate, usually making them hypermetric (too large). This leads to macrosaccadic oscillations sometimes in which the eye overshoots the target each time the patient tries to refixate. If the Cerebellar disorder affects the tuning of the step, it may lead to a post-saccadic drift.

Brainstem lesions affecting saccade accuracy usually make them hypometric (too small).

Visual Field Defects can also cause saccades to be the wrong amplitude, as patients will try to keep a target away from a scotoma or hemianopic field.

Cerebral Cortical lesions in one hemisphere can affect saccade amplitude by biasing saccades toward the side of the lesion, especially vertical saccades which normally require a balanced signal from both hemispheres.

Initiation Disorders

These are conditions which affect the ability to start a saccade, usually showing up as an increase in latency.

Visual Disfunction can lead in increased latencies if targets have reduced visibility as a result.

Attentional Deficits can lead to an absence of voluntary saccades, although reflex saccades may be spared.

Ocular motor apraxia is a condition in which quick phases of nystagmus and reflex saccades are normal but voluntary saccades are delayed. This can be congenital or aquired, and in the latter case usually involves damage to the cerebral hemispheres. Patients with Ocular Motor Apraxia will often use blinking or rapid head turns to facilitate saccade initiation.

Alzheimer's, Parkinson's and Huntington's Diseases all affect voluntary saccades selectively over reflex saccades. This shows up particularly when the patient tries to anticipate a saccade.

Schizophrenia sometimes causes excessive anticipation of saccades when the target location is known in advance.

Inappropriate Saccades

These are conditions in which saccades occur at the wrong time, particularly when trying to fixate steadily. They are also called **Saccadic Intrusions**. When they occur repetitively they may look like nystagmus, but they don't have a slow phase in one direction.

Excessive Distractability describes a condition in which a patient makes reflex saccades to targets when they are trying not to. This shows up in the anti-saccade task as a difficulty in looking away from a flashed target.

Macrosaccadic Oscillations refer to movements which overshoot the target to such a degree that the patient's gaze keeps hopping back and forth across the target. These movements have a relatively normal intersaccadic interval. The amplitude will tend to vary over the course of several oscillations.

Square Wave Jerks are similar in their waveform, but they occur as sudden saccades away from a point of fixation and then back again. These occur in normal individuals but are usually very small and will only be seen under ophthalmoscopy. When they are pathologic, they are more in the range of 1-5 degrees and are more frequent. The amplitude of these movements tends to be more consistent, helping to distinguish them from Macrosaccadic Oscillations. These occur in a wide variety of neurological disorders, such as Cerebellar disease and Progressive Supranuclear Palsy. In some cases they may be very large (10-40 deg) in which case they are called **Macro Square Wave Jerks**. These may occur in multiple sclerosis, for example. Square Wave Jerks also have a relatively normal intersaccadic interval.

Ocular Flutter is characterized by rapid back and forth horizontal saccades without an intersaccadic interval. They occur one right on top of the other. Many people can make these movements voluntarily, in which case it is called voluntary nystagmus. It isn't really nystagmus, because there is no drift component- the person makes saccades in both directions.

Opsoclonus (aka **Saccadomania**) is a condition which is similar to Ocular Flutter, but the movements are large and go randomly in all directions. Again, in this case there is no intersaccadic interval. Both Ocular Flutter and Opsoclonus are usually related to brainstem disfunction, sometimes caused by a tumor or by a viral infection. Certain toxic substances such as thallium and toluene can also produce Opsoclonus or Flutter.