Why do we make saccadic eye movements?

Yarbus 1967
Saccades – Salient Features

- Generated in response to positional retinal error
- Extremely fast - Up to 800 deg/sec;
- Accurate - Gain ~0.9
- Duration - ~30-50msec
- Latency is ~200msec
- Conjugate eye movement
Saccadic Main Sequence Relationships

- Well-defined relationships between saccade metric parameters.
- Usefulto summarize saccadic behavior and quantitatively differentiate between normal and abnormal saccadic behavior.

\[ PV = PV_{\text{max}}(1-e^{-Amp/C}) \]
\[ \text{Dur} = D0+D1\times\text{Amp} \]

Saccade Latency

- Latency is the time taken between the appearance of a target and the eye movement to the target.
- Average saccade latency is around 200msec; slightly faster in a monkey.
- Cortical and sub-cortical processing related to visual processing, target selection and motor programming contributes to latency.
- Under certain conditions saccades can be of ultra-short latency (~80ms) and these are express saccades.
Saccadic Control - Brainstem

- Network of neurons in brainstem control saccade metrics (velocity, amplitude duration)
- Excitatory Burst Neurons (EBN) in the Paramedian Pontine Reticular Formation drive horizontal saccades
- EBN in rostral interstitial medial longitudinal fasciculus (riMLF) drive vertical saccades
- Lesions in these area will abolish saccades in a particular plane

(Kandel, Schwartz, Jessell 4th ed)

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Saccadic Control - Brainstem

- Inhibitory and excitatory burst neurons in PPRF
- EBN firing correlated with saccade velocity
- IBN firing inhibits the contralateral abducens nucleus
- Omnipause neurons (OPN) keep burst neurons silent until a saccade is generated
- Long-lead burst neurons (LLBN) project to EBN and OPN and could provide a trigger signal

(Kandel, Schwartz, Jessell 4th ed)
Example: Saccade Burst Neuron

Saccades-Cortical & Cerebellar Areas

- A number of cortical and cerebellar areas control other aspects of saccadic eye movements such as
  - Sensorimotor Transformation
  - Target selection
  - Attention/Intention
  - Adaptation
  - Sequences/Planning
  - etc

(Kandel, Schwartz, Jessell 4th ed)
Superior Colliculus

- Dorsal mesencephalon
- Part of retino-geniculocortical pathway & retino-tectal pathway
- Layered structure
- Superficial layers – topographically organized visual map
- Intermediate and deeper layers – topographic motor map

Superior Colliculus (cont.)

- Visual and Motor maps in the SC are in register and encode contralateral visual space and contralateral saccades
- Functions of the Superior Colliculus
  - Controls LLBN
  - Rostral zone of the SC promotes fixation
  - Provides information on target goal
  - Involved in target selection
Saccades-Cortical & Cerebellar Areas

- **FEF**
  - Rostral bank of arcuate sulcus
  - Excites SC directly
  - Releases SC from Basal Ganglia inhibition
  - Projects directly to reticular formation
  - Lesions of SC and FEF abolishes saccade generation

(Kandel, Schwartz, Jessell 4th ed)

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Saccades-Cortical & Cerebellar Areas

- **Basal Ganglia**
  - Inhibits SC

- **PPC** – Attention/Intention; priority map

- **SEF**
  - Learned sequences

- **Vermis and Fastigial Nuclei in CBM**
  - Accelerates contralateral saccades
  - Provides a late brake to ipsilateral saccades
  - Saccade adaptation

(Kandel, Schwartz, Jessell 4th ed)
Effect of lesion of Fastigial Nucleus in a monkey

Smooth-Pursuit: Tracking a smoothly moving object

- Generated in response to retinal image motion
- Match eye velocity to target velocity; target velocities can be up to 90 deg/sec
- Latency about 130 msec (compare this to VOR and saccades)
- Accuracy of SP is determined by its gain; SP Gain $\rightarrow$ Eye Velocity/Target Velocity
- Unlike VOR and OKN, SP is not a reflexive eye movement
- Unlike saccades, SP is not an open-loop response
Frequency Response – Smooth-Pursuit Bode plot

- Quality of the smooth-pursuit response decreases (Low gain and increasing phase shift) with increasing frequency of target motion
- Phase shifts suggest that the brain is unable to compensate for latency at higher frequencies

(Das et al 1998)

Pursuit Drivers

- Target velocity
  - Most important. Goal is to match eye velocity to target velocity. The step-ramp stimulus is evidence for the importance of target velocity
Reconstructed target motion

Retinal Error Velocity = Target velocity – Eye velocity

Retinal Error Velocity + Efference copy of Eye Velocity = Reconstructed Target Velocity

Input to the smooth-pursuit system is Reconstructed Target Velocity

Smooth-Pursuit CorticoPontoCerebellar Pathway - Cortex

- Motion sensitive area MT decodes parameters of retinal motion such as speed and direction
- MST contains retinal and extra-retinal information and might encode reconstructed target motion in space
- MST is further divided into two
  - MSTd cells have large receptive fields and likely important for encoding visual motion during self-movement
  - MSTl cells are likely for foveal SP

(Kandel, Schwartz, Jessell 4th ed)
Smooth-Pursuit CorticoPontoCerebellar Pathway - Pons

- The Dorsolateral Pontine Nucleus (DLPN) and the Nucleus Reticularis Tegmenti Pontis (NRTP) are major pontine relay nuclei that channel cortical smooth-pursuit related information to the cerebellum.

Smooth-Pursuit CorticoPontoCerebellar Pathway - Cerebellum

- DLPN and NRTP projects contralaterally to Floccular and Vermal Complex in cerebellum.
- Flocculus and Ventral Parafocculus are likely involved in adaptation of pursuit signals.
- Vermis and fastigial nucleus likely involved in accelerating/decelerating the eye during an ongoing pursuit movement.

(Kandel, Schwartz, Jessell 4th ed)
The aVOR

- Gaze holding mechanism that generates eye movements to compensate for head motion

- Gaze or line of sight is maintained on a stationary target

Bode plot of VOR performance

- During locomotion head frequency is 1-5 Hz and head velocity is <150 deg/sec

- VOR performance is optimal for these stimuli
Bony and Membranous Labyrinth

- Inner ear contains the structures responsible for the VOR
- Inner ear is called the labyrinth because of the complexity of its shape
- Outer part is called the Bony Labyrinth
  - Series of cavities inside the petrous portion of the temporal bone
  - Contains perilymph which is similar to cerebrospinal fluid
  - The temporal bone of the bony labyrinth is one of the hardest bones of the human body
- Inside the bony labyrinth is the membranous labyrinth
  - Takes the same shape as the bony labyrinth
  - Separated from bony labyrinth by perilymph

Membranous Labyrinth
- Cochlea
- Otoliths
  - Utricle
  - Saccule
- Semicircular canals
  - Horizontal
  - Anterior
  - Posterior
Semicircular canals sense angular head acceleration

- Thin tubes that contain fluid called endolymph
- At the base of each canal is an enlarged region called the ampulla
- Inside the ampulla is the crista. Cristae of each canal contains hair cells.

Mechano-electric transduction by Hair Cells
• Processes of hair cells are embedded in the cupula which lies in the ampullae

• Cupula is gelatinous membrane that prevents the free flow of endolymph

How do the SCC sense head motion?

• Acceleration of the head results in movement of fluid in the SCC.

• As the head rotates in one direction, inertia of the fluid causes it to lag, and hence generate relative motion of the endolymph in the SCC.

• Motion of the endolymph results in the bending of the cupula and therefore also bending of the stereocilia of the hair cells.

• Bending of the stereocilia results in depolarization or hyperpolarization that is a function of the head motion.
Vestibular Nystagmus (VN)

- Sustained head rotation results in VN
  - Physiological VN that decays with time
- Vestibular imbalance can cause VN
  - Pathological VN
  - Reducing a signal from one canal is responded to as if the opposing canal were being stimulated
  - Eyes drift toward side with lesion.

Canal Planes

- Canals work in push-pull
  - Advantage of push-pull is that in case of disease that destroys one labyrinth, the other side can take over (e.g., ear infection)
- Left AC is parallel to Right PC
- Push-pull pairs
  - RLC & LLC
  - RAC & LPC
  - RPC & LAC
3-neuron arc

- Latency of VOR is short because there are only 3 neurons between input and output
  - Neuron 1: Canals -> Vestibular Nucleus
  - Neuron 2: Vestibular Nucleus -> Abducens Nucleus
  - Neuron 3: Abducens Nucleus -> Oculomotor nucleus
- 4 Vestibular nuclei – Medial, Lateral, Superior and Inferior

Vision and the VOR

- In resting state VOR gain is about 0.8-0.9
- In the presence of a visual target, gain goes upto 0.95-1.00
- This visual enhancement is believed to be due to the SP/OKN system
- This is called the visually enhanced VOR (Vis-VOR)
Otoliths transduce linear head motion and gravity

- Utricles and Saccules
- Utricles primarily sense tilt (gravity) and horizontal linear acceleration
- Saccules primarily sense vertical linear acceleration
- Saccule is parasaggital; Utricle is horizontal

Macula are the equivalent of the cristae and contain hair cells
- Hair cells in the macula are oriented in various directions
- Processes are embedded in otolithic membrane
- Calcite crystals called otoconia are strewn on otolithic membrane
- Saccule – lateral SVN; Utricle – laterodorsal MVN and ventrolateral SVN
What is the OKR?

- The optokinetic reflex (OKR) is a visually driven eye movement that helps to stabilize the retinal image during large-field motion.
- This reflex generates a nystagmus-like eye movement in response to a unidirectional motion of the visual world called optokinetic nystagmus (OKN).
- [Optokinetic Nystagmus - YouTube](#)
- OKN slow phase is in direction of the motion of the stimulus and the quick resetting phase is in the opposite direction
- The OKR complements the VOR at low frequencies of head rotation

Components of OKN

- Initial rapid rise in OKN slow phase velocity followed by gradual increase to steady state
- Gain of OKN defined as the ratio of steady state eye velocity to stimulus velocity is close to 1.0 for stimulus velocities up to 90 deg/sec

(Cohen et al 1976)
Slow and quick phases

- Convert position to velocity by differentiation
- Slow phases are the important phase that minimize retinal slip
- Quick phases are the resetting phase

Optokinetic after-nystagmus (OKAN)

- OKAN refers to the persistence of nystagmus after the OKN stimulus is removed and the subject is placed in darkness.
- There is a initial rapid drop in eye velocity followed by a more gradual decay of eye velocity
- Sometimes there is a reversal of the nystagmus after OKAN and this is called OKAAN (rare).

(Cohen et al 1976)
Vestibular-Optokinetic interaction

- Thus during sustained rotation in the light, OKAN cancels PRN

Example of vergence eye movement

Vergence position = LE position – RE position

Therefore, convergence is positive and divergence is negative
Near Triad

- Convergence is accompanied by increase in accommodation and pupillary constriction
- Accommodation is necessary for changing focus on viewing a near object
  - Brought about by changes in lens shape
- Pupillary constriction helps to increase depth of field thereby reducing the amount of accommodation needed
- Cross-coupling between vergence and accommodation control systems

Stimulus to Vergence – Retinal Disparity

- If retinal disparity is non-zero, it means that the image is falling on non-corresponding retinal areas.
- A crossed disparity gives rise to perception of ‘near’ and is the stimulus to convergence.
- An uncrossed disparity gives rise to perception of ‘far’ and is the stimulus for divergence.
- Thus, retinal disparity drives a form of vergence called fusional vergence or disparity vergence.

(Adler’s Physiology of the Eye)
Stimulus to Vergence – Retinal Blur

- When an object is brought closer to the subject, it appears blurred because the subject is focused behind the object.
- The subject must engage accommodation mechanisms to clear blur.
- Due to the linkage between accommodation and vergence systems, this also induces a vergence eye movement.
- Thus blur drives a form of vergence called *accommodative-vergence or blur vergence*.

Vergence and Accommodation Cross-coupling models

- A blur stimulus can drive vergence via an accommodation-vergence crosslink; The strength of this crosslink is defined by the AC/A ratio.
- A disparity stimulus can drive accommodation via a convergence-accommodation crosslink; The strength of this crosslink is defined by the CA/C ratio.
Accommodative-Vergence has different dynamics than Fusional-Vergence

Accommodation (diopters) - Vergence (MA)

Monocular Viewing

Binocular Viewing

Accommodation stimulus ($A_d$) and response ($A_r$), vergence stimulus ($V_d$) and response ($V_r$), and horizontal position of the right eye ($R$) in response to steps from 0 D to 3 D and back of a target moving directly toward and away from the right eye in a plane parallel to the midline. $V_r$: responses during binocular viewing. Vergence and right eye position are plotted in meter-angles (MA) so as to be commensurate with accommodation (diopters). Monkey 1.

(Cumming and Judge 1986)

Dynamic properties of vergence eye movements – Main Sequence

A. Vergence Velocity

- Convergence may be faster than divergence
- Divergence speed depends on initial vergence position

(Maxwell, Tong, Schor 2010)
How does the brain generate eye movements in depth (3-D)?

• In a framework proposed by Hering, vergence is an independent eye movement subsystem and is controlled separately from conjugate eye movements such as saccades.

• An eye movement made in response to a stimulus that both changes in depth and conjugate position is a simple sum of separately generated vergence and conjugate movements.

How does the brain generate eye movements in depth (3-D)?

• Vergence is defined as LE position minus RE position
• Conjugate movement is defined as average of RE and LE positions.
• If the composite movement is the sum of vergence and conjugate components, then movements of each eye is as follows
  – RE = Conjugate - Vergence/2 ;
  – LE = Conjugate + Vergence/2
• In the alternative framework proposed by Helmholtz, each eye is controlled independently.
• There is evidence supporting either framework; however the Hering framework is more useful clinically.
How are eye movements in depth controlled – Hering’s framework

• Separate conjugate and vergence components of eye movements are summed at the level of motoneurons

Gamlin and Mays, 1992
Vergence Signals in the Brain – Supraoculomotor Area (SOA)

- Midbrain near response cells in the supraoculomotor area (SOA)
- 1-2mm dorsolateral to oculomotor nucleus
- Monosynaptic connections to medial rectus motoneurons

Mays, J. Neurophys 1984
Support for Hering’s Hypothesis – Internuclear Ophthalmoplegia

(Movie from Leigh&Zee (1999) 3rd edition)

Vergence in other parts of the brain - cortex

- Disparity encoding (sensory)
  - V1
  - MT/MST
  - LIP
- Vergence eye movements (motor)
  - FEF
    - Vergence neurons are adjacent to the saccade neurons in the FEF
  - SEF
    - Perhaps important for predictive vergence eye movements
Vergence in other parts of the brain - cerebellum

- Dorsal vermis
  - Lesions here cause esodeviation, variation of alignment with orbital position, disconjugacy of saccades and problems in phoria adaptation
- Fastigial Nucleus and Posterior Interposed Nucleus
  - Receive projections from the vermis
  - Project to the SOA
  - FN has neurons related to convergence
  - PIN has neurons related to divergence
- Cerebellar flocculus
  - Also has neurons related to vergence but is most likely important for changing VOR gain with vergence angle

Neural control of vergence - new evidence

- It appears that the framework may not be as Hering proposed
- Pre-motor drive is monocular (Helmholtz)
  - Neural recordings in the PPRF during asymmetric vergence suggests that these cells encode movements of a single eye rather than a conjugate signal
An amalgamated framework for binocular control

- ‘Fast’ and ‘slow’ vergence systems
- Fast vergence uses mostly monocular circuits (Helmholtz-like)
- Slow vergence necessary of vergence pursuit, fine tuning of binocular position after fast component and static alignment is mostly binocular (Hering-like)

Asymmetric vergence

- Neural responses in many oculomotor areas (PPRF, NPH, SC) during asymmetric vergence tasks suggests that there is some level of monocular encoding.
- Fast vergence may be different from slow vergence
  - Slow vergence obeys Hering’s framework
  - Fast vergence shows facilitation and aspects of monocular encoding
Summary

• Why study the neural control of eye movements?
  – Vision and eye movements are a window into the brain
    • From sensation to action
  – Simple and elegant model for neural control of movement
    • No stretch reflex; Unchanging mechanical load
    • Movements restricted to three planes
  – Independent subsystems classified depending on function
  – Clinically, many abnormalities are associated with clear pathophysiology