**Exp. Ch 3: Can saccadic adaptation lead to improvements in both action and perception?**

The previous chapter showed that prism adaptation failed to improve performance on SWM and temporal estimation tasks. The suggestion here is that prisms influence dorsal stream functioning and that both these tasks rely, at least to some extent, on ventral stream processes.

Prism adaptation by design influences both visual and proprioceptive frames of reference   
(Redding and Wallace refs - 2006). In fact, depending on the specifics of the adaptation protocol, the bulk of the influence of prisms is seen on proprioceptive tasks (refs).

After-effects tend to be about 40% of the shift; vision account for around 10% of the after-effects and proprioception the rest. [don’t use actual numbers – “Depending on the procedure employed, the bulk of the after-effect is seen in a proprioceptive reference frame. Might need to address what we did – concurrent feedback? So that procedure does not bias towards proprioceptive changes as dramatically as terminal feedback but could still be biased in that direction]

[Prism adaptation and unilateral neglect: review and analysis.](http://www.ncbi.nlm.nih.gov/pubmed/15907951)

**Redding** GM, **Wallace** B.

Neuropsychologia. 2006;44(1):1-20.

[Applications of prism adaptation: a tutorial in theory and method.](http://www.ncbi.nlm.nih.gov/pubmed/15820548)

**Redding** GM, Rossetti Y, **Wallace** B.

Neurosci Biobehav Rev. 2005 May;29(3):431-44.

[Long-lasting aftereffect of a single prism adaptation: shifts in vision and proprioception are independent.](http://www.ncbi.nlm.nih.gov/pubmed/16552560)

**Hatada** Y, **Rossetti** Y, Miall RC.

Exp Brain Res. 2006 Aug;173(3):415-24.

Why would changes in a proprioceptive frame of reference lead to after effects influencing visual perceptual representations?

Saccadic adaptation offers an alternative approach to rehabilitating neglect that may overcome some of the shortcomings of prism adapation.

[describe saccade adaptation procedure and classic results]

Saccadic adaptation operates in a retinocentric co-ordinate reference frame (refs).

Inducing changes in a retinocentric frame of reference could potentially influence a broader range of behaviours important for both attention and the accurate construction of perceptual representations.

**the accurate construction of perceptual representations**

Saccades are precise motor movements that are usually programmed to move the eyes to foviate a specific target. Saccadic suppression, and the speed limitations of retinal cells, prevent visual information from reaching the brain during the movement [@Matin1982], and thus the brain from making on-line motor corrections, and yet, the eyes land reliably close to the target most of the time. This ability to execute a pre-programmed motor movement with extreme precision, reliably, and maintain that ability over a lifetime, despite operating, essentially "blind," is a testament to one or more highly capable underlying control systems.

**Could condense the above to a sentence.**

[accuracy is maintained through adaptation] Any motor system must incorporate a realistic expectation of inaccuracy, and perform in way that minimizes consequences. Because on-line feedback is not available in this particular case, the visual motor system is forced to rely on information gleaned after-the-fact, or, in other words, "error signals," to maintain effective control mechanism parameters [@Wong2010]. There exists a rich, half-century of investigation into this short-term parametric adaptation of saccades, or simply "saccadic adaptation," based on the original paradigm developed by @mclaughlin1967. Saccadic adaptation tasks mimic and amplify oculomotor processes that occur naturally and on a continual basis in humans. For example, neuromuscular changes, such as a changes in the strength and function paresis of ocular muscles due to paresis, injury [@Kommerell1976], or aging [@warabi1984], or the wearing of magnifying glasses [@Erkelens1989], result in some saccadic error, and the neuroplasticity underlying saccadic adaptation permit correction so that vision is not impaired. These types of perturbations can be monocular or binocular [@Erkelens1989] and can effect saccadic accuracy in various dimensions[@Chaturvedi1997].

**Condense the above – pair it with the sentence describing a saccade and have the main point simply be – the system can adapt. “… adapts to a wide range of perturbations.”**

[SA is motoric, but also perception -compare with prisms] From the earliest discussion, saccadic adaptation has been compared to prism adaptation and other examples of sensory-motor neural plasticity [@mclaughlin1967]. Two characteristics make it unique. First, as mentioned above, unlike other adaptive systems, saccadic adaptation is unable to rely on feedback, due to the saccadic suppression. Second, it straddles the perceptual and motor systems in a highly unique way. Saccadic adaptation *is* a form of sensory adaptation, because it changes the way the environment is perceived. Vision is entirely dependent on where the eyes look, so when eye movements change, the input to the visual systems are directly changes. At the same time saccadic adaptation *is* motor adaptation, as it is fundamentally the parameters of motor movements, not sensitivity, that is adapted. Prisms are similar, but involve different systems. While SA effects the motor plan to execute a saccade to a particular point in a person's visual periphery, Prisms don't change eye movements. Instead, they shift the ocular position of "straight ahead" in body-centric terms.

**Keep the above – reads well**

## Perceptual Effects of Saccadic Adaptation

### Transient modifications of spatial perception occurs around saccade

[By nature, saccades influence perception] Saccades are the motor action that has the potential for the strongest influence on visual perception. Eye movements are continually responsible for the content of what is fed to the perceptual streams, as they direct our gaze and dictate where and when we acquire the visual information which provides the pieces with which we construct our internal representation of the visual world. In a complementary way, saccades have the ability to *mask* large changes in the visual scene through saccadic suppression, producing a perceptual system that is, in a way, forever subservient to action systems.

FIXME: Useful?: Eye movements are strongly coupled to goal-direction actions [@Neggers2001GazeAnchoring!].

[SA can bias perception] One way the effects of saccadic adaptation on perception may be measured is by trying to induce perceptual biases in the adapted field. In an early such task, @Mack1978 found that when a vertical gain was added to horizontal saccades by perturbing lateral targets upward, participants became desensitized to upward motion and sensitized to downward motion. In other words, their threshold for detecting upward motion was increased, and downward motion, decreased [@Mack1978].

Another way of examining the way saccadic adaptation can bias perception is to test subjective judgment of the locations of targets in the adapted field. is by testing for mislocalization of targets in the adapted field. @Zimmermann2009

@Hernandez2008 found that saccade lengthening (but not shortening) transferred to pointing gestures to flashed targets. They try to account for the effect as a combination of retinal location, sensorimotor transform of retinal-to-extraocular muscles (of an encoded saccade), and eye position. They postulate that the saccade lengthening adaptation modifies TODO:understand this paper.

[are the effects transient or lasting?] [@Alahyane2005]

### Lasting after-affects on Perception are more subtle, but may exist

[2 basic types of enduring effects. Attention and motor transfer]

[SA-like adaptation of covert attention is possible] Interestingly, @McFadden2002 found that they could directly adapt attentional deployment in the absence of any eye movement. They cued attention to a peripheral location, and then perturbed the cue back toward fixation at a time interval estimated to coincide with an attentional shift. They found that attentional shifts became gradually reduced. They also found that when the participant was allowed to make eye movements, the adaptation had transferred to saccades as well [@McFadden2002]. FIXME: and this is important why?

## Saccadic Adaptation for Patients with Perceptual Biases

[SA has untested potential for perceptual disorders] While other tasks with similar heritage, like prism adaptation, have been extensively used in clinical research applications, saccadic adaptation has remained predominantly in the realm of psychophysics and tk (healthy participants). There are some exceptions, mostly in disorders involving cerebellar degeneration, but generally, the task may be an un-examined "gold mine tk" for understanding perceptual and vision disorders.

[precedent for clinical application]

* Briefly mention the use of SA in hemianopic patients [@Lvy2012] and abnormal eye movements during reading [@Desestret2013]

[potential future research directions]

* wide area adaptation [@Garaas2008]
* Concluding section should include possible experimental directions **and** drive the point home that this could be an untapped source of information about spatial cognition and potential clinical application.

[describe current project]

**METHODS, Results Discussion**

Qualitative description of case study: Launch the argument here that failures (in SA and PA) are due to techniques that influence reflexive, reactive mechanisms. Another point to make here is that neglect patients never say there’s anything unusual about the prisms – that is, they are not aware of the shift despite adapting to it – more evidence that the effects are implicit.

[brief description of patient and protocol; brief description of results; could you make a figure that has eye traces for controls vs. eye traces for Brian?]

Perceptual effects of SA

[SA involves a complicated set of mechanisms] It would be easy to assume that saccadic adaptation occurs by the integration of a relatively simple "error signal" into a type of universal saccadic "gain" parameter. Ultimately, this does not appear to be the case. There is, in fact, more than one type of error signal that the brain could make use of, from motor afferent signals and the visual system, as well as several possible parametric ways of changing saccade amplitude [@Lappe2009]. This complex set of features make saccadic adaptation an interesting way to investigate functional plasticity mechanisms in the brain, and provides a clear contrast with prisms, for which the updating mechanisms are not functionally equivalent. This comparable, but functionally different response to saccadic relative to prism adaptation may provide a profitable avenue for investigating, or even ameliorating the asymmetrical attention problems in people with Unilateral Neglect or other related disorders.

### Volitional and Reactive Saccades are Distinct

[Intro, reactive/express] Saccades, generally, can be subdivided into two types based on function. Humans and most other visual animals respond to sudden changes in peripheral space by orienting, and typically foviating the stimuli. This is necessary in humans because of impoverished retinal resolution and perceptual information processing in the visual periphery. The need to quickly assess environmental changes provides a universal drive to orients accurately and quickly toward such stimuli, with little top-down interference.

[Volitional/endogenous] In contrast, self-directed investigation of an environment by goal-directed, internally initiated saccades, such as in visual search, requires a somewhat different strategy. Such saccades are, by definition, going to involve a greater degree of entanglement with conscious goal-monitoring mechanisms, and other high-level cognitive systems. As such, unlike reactive saccades, these voluntary saccades are very likely to involve move extensive functional brain areas, and exhibit somewhat different characteristics. Besides different functional brain structures, volitional and reactive saccades, also called targeting and express saccades, respectively in the literature, present different behavioural characteristics. For example, reactive saccades exhibit very short latencies when compared with volitional saccades [@Alahyane2007].

#### Different Systems and Properties.

[structural distinction] Saccades triggered by exogenous cues, like a sudden movement or appearance of an object in the periphery are considered reactive saccades and are typically contrasted with voluntary saccades. Reactive saccades have much shorter latencies (as short as 100ms in humans), and are therefore thought to involve a smaller neural architecture, perhaps restricted to early visual areas, superior colliculus, and brain-stem [@Fischer1993]. Voluntary saccades are the type of normal eye movements performed based on the execution and monitoring of internal goals like searching for an object or monitoring the progress of a manual task. While this distinction is less clear in the cerebellum, it does seem to explain a degree of functional specialization in the oculomotor areas of the cerebral cortex [@Schraa-Tam2009,@Johnston2008,@Müri2008] and contribution of the superior colliculus [@Schiller1987].

[SC] Animals with lesioned superior colliculus are unable to perform reactive saccades, but retain the ability to generate saccades endogenously [@Schiller1987]. When the frontal eye fields are also lesioned, they lose this ability as well [@Schiller1987], indicating unique structural dependencies for the two types of saccade. As a result, it's valuable to keep in mind the distinction when comparing results from experiments which may be utilizing different saccade types, and when attempting to extrapolate mechanistic models based on simple reactive saccades to more naturalistic behaviour.

[Cortex] @Schraa-Tam2009 used fMRI imaging to investigate the neural correlates of saccade generation. In a direct comparison, self-paced, voluntary eye movements elicited significantly different activation of several cortical areas, including frontal eye fields, parietal eye field, area MT/V5, the precunious, the angular and cingulate gyri, but no change in cerebellar regions [@Schraa-Tam2009] . While area MT/V5, or the motion sensitive area, was likely triggered because of the slight difference in stimuli required to elicit reactive saccades, the other activations indicate substantially unique cortical activation for voluntary verses reactive saccades. This supports other research done with primates that finds similar results [@Johnston2008]. A review of lesion and TMS research by @Müri2008 also singles out the frontal eye fields as being a critical component unique to voluntary saccades [@Müri2008].

FIXME: If needed, papers examining the differing cognitive mechanisms and behavioural characteristics (but not neural substrates) between reactive and voluntary saccades [@Alahyane2007, @Collins2006, @Cotti2007, @Cotti2009, @Deubel1995, @Erkelens1993, @Fujita2002, @Zimmermann2009].

[caution when extrapolating or comparing the two] An appreciation for the behavioural and functional differences between voluntary and reactive saccades should inform any discussion of saccadic adaptation. Most research into saccadic adaptation involves the adaptation of reactive saccades, and there is a danger of overgeneralizing results from this work to all eye movements. Results from the adaptation of volitional saccades, or better yet, from research involving both types of saccades, are always going to give a more reliable picture of the mechanics of maintaining the effectiveness of voluntary eye movements.

## Saccadic Adaptation Paradigm and Established Results

### Adaptation is not generalized

[position and direction specificity] Some of the most reliable characteristics found when investigating saccadic adaptation are direction and magnitude specificity. While adaptation seems to generalize to any starting eye position, only saccades similar to the trained vector direction and magnitude show effects [@Miller1981;@Frens1994;Noto1999;@Alahyane2004;@Alahyane2003]. Interestingly, the same lack of transfer can be found from one point to another at a different depth in 3D peripersonal space [@Chaturvedi1997]. Others have found that when adapted in one meridian, there is limited transfer to others [Lemij1992]. There also seems to be nearly strict independence of horizontal and vertical adaptation [@Watanabe2003]. Adaptation of a particular saccade amplitude do not generalize to other amplitudes [@Miller1981;@Frens1994;@Albano1996;@Straube1997]. And, perhaps the most reliable and long-observed specificity is directional. When, for example, leftward saccades are augmented or reduced with saccadic adaptation, rightward saccades are unaffected, regardless of the spatial position overlap [@Deubel1986;@Frens1994;@Albano1996].

[Rather than Cartesian specificity, spatial reference frames] The different dimensions of adaptation described above can be re-phrased in terms of spatial reference frames. Particular locations in retinal space could be considered orbitocentric or retinocentric, depending on whether starting position matters, while directional effects, or differences between saccade reduction and augmentation can be thought of as oculocentric. Saccadic adaptation seems to function in a way that is primarily retina-referenced, rather than an orbitocentric [@Albano1996]

@Albano1996 had participants observe targets as they were displaced horizontally across a computer scree, and indicate whenever the target dimmed. The final position of one trial became the starting position of the next, so that to the participant, the target seemingly moved randomly back and forth across the screen. Intrasaccadic target displacements were made in order to induce saccadic adaptation. They were always horizontal, and when they occurred, always a 40 percent change, either more or less than the initial saccadic distance at the beginning of the trial. The resulting data

#### Augmentation and reduction are probably uniquely specialized.

[+-gain is important distinction]Probably the most extensively studied dichotomy(?) of saccade adaptation is the difference between tasks that lengthen or shorten saccades. Over the storied history of research into the distinction, it has been referred to as augmentation and reduction, outward and inward adaptation, forward and backward adaptation, as well as potentiation and depression. Regardless of the terminology, the systematic intrasaccadic perturbation is nevertheless designed to cause either over-shooting or under-shooting of saccades relative to the targets, and over the course of training, inducing hypometria or hypermetria of saccades, even later, in the absence of further target perturbations. Most saccadic adaptation research involves only one type, but experiments comparing the two have found that saccadic augmentation and reduction may involve distinct, or at least partially distinct, mechanisms, exhibit different behavioural characteristics, and serve somewhat different functions [@Catz2008, @Golla2008, @Hernandez2008, @Panouillères2009, @Panouillères2012].

[Distinct systems]Experiments that have examined both backward and forward adaptation have found that backward adaptation is considerably more robust, occurring in fewer trials, and is more reliable from person to person [for a review, see @Hopp2004]. They also appear reflect structurally unique systems. For instance, @Panouillères2009 adapted participants either forward or backward, and had them perform anti-saccades toward the adapted location. While most participants adapted to their assigned conditions (5 of 19 in the forward condition did not), only the backward adapted participants exhibited transfer to anti-saccades. This hints that backward adaptation is occurring after the mechanism required for saccade inversion, while forward adaptation may not. Furthermore, @Panouillères2012 followed up with Transcranial Magnetic Stimulation (TMS) of the lateral cerebellum during the adaptation phase of both adaptive lengthening and shortening of saccades. The result was a potentiation of adaptive lengthening, and and a depression, and near elimination, of saccadic shortening, providing a neuroanatomical disassociation between the two [@Panouillères2012] . Cellular recording of primates seems to support this notion of divergent neuroanatomy for the two types of adaptation. For instance, the population response of Purkinje cells in the cerebellum seems to encode or influence the duration of normal and gain-increased saccades, but not gain-decreased saccades [@Catz2008].

[Why? Shortening is fatigue and may be special] There are a variety of reasons for oculomotor systems to become more error-prone. One particular, natural, cause, is both likely to be both ever-present and unidirectional in the error it produces. Muscular fatigue is presumably a major contributor to an organism's need for adaptive mechanisms. Unlike, for example, damage to a particular muscle, or other biomechanical changes, fatigue is always going to reduce saccadic amplitude, regardless of the direction of the saccade. It stands to reason that a "fatigue coping" system, because it is going to be continually engaged, may be different in some ways than the mechanisms for lengthening, or augmenting, saccades over time. In fact, its possible that part or even all of saccadic reduction could be accounted for by uncompensated fatigue. Backward perturbations remove the error signal that engages anti-fatigue adaptation, and as a result, saccades may shorten as a result of fatigue rather than any particular active adaptive mechanisms. Beyond that, for whatever reason, normal saccades are hypometric [@Wong2012]. As a result, backward adaptation is unique in that occurs with target perturbations that either reduce the "error" in foviating the target stimulus, or actually reverse the typical error signal by producing an artificially hypermetric saccade.

[Vermal patients cant compensate for fatigue or adapt to SA] @Golla2008 tested controls and patients with cerebellar damage on a saccadic adaptation task involving both augmented and shortened saccades. The controls, and two patients with an intact oculomotor vermis, but large, unilateral hemispheric lesions, adapted to the augmentation by increasing saccade duration, but not peak velocity. They adapted to inward adaptation, in a different manner by exhibiting changes both parameters. In contrast, patients with damage to the oculomotor vermis exhibited a complete extinction of outward adaptation, and a partial loss of inward adaptation. Tellingly, they were also unable to reliably saccade to un-perturbed targets over time as well. They exhibited a lack of resilience when asked to saccade to fixed targets repeatedly. Their saccades to these steady-state targets decreased in duration, producing saccades which were more and more hypometric as the task went on [@Golla2008] . This does not appear to the result of an unprocessed error, as these poorer and poorer saccades were followed by a necissary increase in corrective saccades [@Golla2008]. Instead, when taken together, the selective, partial retention of inward adaptation and the gradual shortening of saccades to static targets indicate that rather than active adaptation, these participants are simply failing to adequately compensate for fatigue of some sort.

## Structure of an adaptive system

[Structure of SA comes heavily from animal studies]While variants of the standard target-perturbation based paradigm are the base of research investigating saccadic adaptation, much of the information about the structural functionality maintaining saccadic accuracy come from the effects of lesions or other neural dysfunction, and animal research. Saccadic adaptation is an important low-level function of mammalian visual systems, which all have imperfect ability to produce accurate muscular torque over time, and imperfect perceptual abilities, so animal research can provide a great deal of insight. Two approaches to study saccadic adaptation in animals have typically been used. The more common procedure of perturbing targets during the perceptual blindness of a saccade, and the lesioning of extraocular muscles in monkeys [@Optican1980; @Scudder1998].

### Cerebellum is key to maintaining reactive saccades

[Cerebellum=control] Saccadic adaptation is actually one of a set of adaptation methodologies that has been central to understanding the cerebellum. The cerebellum is a key area for movement control and sensory-motor plasticity [@Glickstein2011]. A full analysis of what is known about the neural substrates of saccadic adaptation in the cerebellum would be beyond the scope of this dissertation. However, the vast majority of neuroscience research investigating saccadic adaptation has investigated, and in-fact implicated, structures in the cerebellum as being either involved-in or directly responsible for the learning the new oculomotor parameters. For more extensive reviews, see @Iwamoto2010 and @Pelisson2010.

[damage leads to loss of control] People with damage to the cerebellum are typically characterized as having loss of movement coordination, or "ataxia" of one movement type or another. A more nuanced view, though reveals two very basic deficits. First, movement precision is poor, with delayed and inappropriate corrections producing oscillations, or "intention tremors", especially for multi-joint complex actions [@Diedrichsen2013]. Secondly, and more directly relevant to the discussion of saccadic adaptation, they typically fail to respond to feedback like that of saccadic adaptation. The intention tremors seem to be related to an ineffective or delayed use of sensory feedback, as it is reduced or absent when patients point to targets with their eyes closed [@Day1998].

[including in SA] Further, cerebellar damage seems to cause a variety of oculomotor deficits, including dysmetria of saccadic eye movements, and Nystagmus, an involuntary eye movement consisting of slow drift and fast resetting phases, as well as an abnormal Vestibulo-ocular- reflex [@Diedrichsen2013]. People with syndromes associated with cerebellar dysfunction also show impaired saccadic adaptation [@Waespe1992]. Similarly, in monkeys, targeted damage to the cerebellum (Oculomotor cerebellar vermis, fastigial nuclei) can nearly eliminate the ability to adapt saccades [@Optican1980; @Goldberg1993; @Takagi1998; @Barash1999]

[Certain regions in particular] Medial, posterior, cerebellum (vermis and fastigial nuclei) is thought to be central in the control of accuracy and adaptive calibration of saccadic eye movements [for reviews see: @Hopp2004, @Pélisson2003, @Pélisson2010]. For example, repetitive transcranial magnetic stimulation of the medioposterior cerebellum has been shown to produce an inhibitory effect on saccadic adaptation [@Jenkinson2010]. Evidence for the role of other areas of the cerebellum is much more sporadic and and difficult to glean a clear-cut role from. Deficits of saccadic adaptation observed in humans with cerebellar lesions suggest possible importance of lateral structures [@Alahyane2008, @Choi2008, @Golla2008, Straube2001]. Some electophysiological studies [@Mano1991, @Ron1973] and imaging studies [@Dieterich2000, @Schraa-Tam2009] have hinted at other parts of the cerebellum being involved in the control of saccades

[The Cerebellum is doing...] The cerebellum hints at a temptingly universal function, occasionally affectionately referred to as the cerebellar transform. It's recursive connectivity with motor, sensory and other areas of the cortex as well as brainstem and direct spinal pathways, as well as it's universal-seeming motor-refining abilities, and uniform but modular histological structure, hint at a general function applied to a wide range of motor actions. Unfortunately, the exact nature of this "cerebellar transform" is a longstanding problem in neuroscience, and goes far beyond what can be discussed here. In brief, it may serve as a "predictive forward model" builder for motor control [@Maill1998], or provide the input to build such models if they happen to be located elsewhere in the cortex. Alternatively, the more classical description of cerebellar function is that of error-based learning [@Marr1969;@Albus1971] originally described a computational model of error-based learning in the cerebellar cortex, and that idea of error-based learning has been adopted as a central notion in research into the cerebellum to date. Unfortunately, the Marr-Albus theories, while recognizing the apparent need for an "error-signal" to drive neuromotor learning, provide only a rudimentary idea of the type and function of that error [see @Highstein2005 for a more recent discussion]. The contemporary idea of error-based learning is based on the comparison of predicted and actual sensory movement outcomes. Crucially, it is the signed difference between those outcomes that is capable of providing the impetus for a lasting parametric adaptation [@Tseng2007].

[Not so simple] Cerebellar lesions can also effectively eliminate prism adaptation, both in terms of corrections to movements while wearing prisms, and any aftereffects [@Martin1996]. Similar results have been found with adapting pointing movements to a force field or perturbations produced by a robot arm [@Maschke2004;@Smith2005], gait adaptation to a split-belt treadmill [@Morton2006], and reaching under novel visuomotor transformations [@Tseng2007]. Saccadic adaptation is thus one of many sensorimotor adaptations that seem to require the cerebellum [@Golla2008, @Prsa2011]. However, even this finding may be influenced by other oculomotor deficits. For example, some researchers have found hypometria but unimpaired saccadic adaptation in patients with diffuse cerebellar atrophy and cerebellar infarction [@Choi2008]. The picture is likely far more complex than the cerebellum, and almost certainly involves a complex interplay with other structures, like the superior colliculus and cortical areas.

#### Cerebellar Vermis and lateral structures

[Cerebellar regions that contribute to SA]The cerebellum is far from a homogeneous structure, and so considerable research has examined the functional anatomy of cerebellar sub-structures. The cerebellar vermis, and more specifically, the vermal lobuli VI and VII, commonly called the posterior, or oculomotor vermis, is probably the best studied and well known contributor to the control of saccadic eye movements. Purkinje cells in this area are sensitive to eye position and, as a population, encode saccade parameters like saccade timing and direction [@Thier2002].

[medio-posterior cerebellum is primary candidate] There is substantial support indicating that that the medio-posterior cerebellum, which includes the above mentioned oculomotor vermis, plus the caudal part of the fastigial nucleus, contributes to saccadic adaptation, or, at minimum, backward adaptation of reactive saccades [@HoppFuchs2004,@IwamotoKaku2010,@Pélisson2010,PrsaThier2011,Tian2009] . For example, patients with lesions of the cerebellar vermis [@Golla2008], or with a neurodegenerative disease which happens to primarily damage the Purkinje cells of the vermis [@Xu-Wilson2009] are unresponsive to backward saccadic adaptation. TODO: Further evidence provided by [@Desmurget1998,@Jenkinson2010] if necissary.

[However, lateral areas may also play a part] It also requires mentioning that there is some evidence of involvement of other parts of the cerebellum in the adaptation of reactive saccades. @Panouillères2012 was able to modify reactive saccade adaptation with transcranial magnetic stimulation of the hemispheric lobule Crus I. Others have found further hints of hemispheric involvement [@Alahyane2008,@Choi2008,@Straube2001,@Broekhoven2009].

[TMS of lat. cerebellum affects SA in complex ways] In order to investigate the involvement of lateral cerebellum, @Panouillères2012 found that TMS over the human left Crus I of the cerebellum after saccade detection had a dual effect on saccadic plasticity. Perhaps paradoxically, after-effects indicated that it both reduced the effectiveness of saccade-shortening adaptation (for saccades moving contralateral to the stimulation), and augmented saccade-lengthening adaptation (for saccades in both directions) [@Panouillères2012]. In addition to affirming lateral cerebellum in saccadic adaptation, this provides further evidence for distinct neural mechanisms of saccadic depression and potentiation, and hints at an antagonistic relationship between the two. Interestingly, the authors also found that TMS immediately at saccade-onset, rather than after a delay, induced hypometria in that same saccade, to a small degree, but consistently in both directions. However, saccades with 30 or 60ms delayed TMS were not measurably effected, however, all three conditions lead to the after-effects described above [@Panouillères2012].

[Structure of Voluntary SA less studied] Much less work has been done examining the neural substrates of the adaptation of volitional saccades, despite the fact that these endogenous saccades are crucial for day-to-day life. Earlier work seemed to indicate that cerebellar lesions affected the accuracy of reactive saccades [@Straube1995], but a more precise understanding probably comes from examining the particular region of the cerebellum damaged. @Alahyane2008 examined deficits in two individuals undergoing both reactive and voluntary adaptation after isolated lesions in medial and lateral parts of the cerebellum. Saccadic adaptation to contralesional targets was normal, however, aftereffects post adaptation to ipsilesional targets depended on lesion location. They found a double disassociation, where the medial lesion degraded adaptation to reactive saccades, but left the voluntary saccade adaptation unhindered, while the lateral lesion left reactive saccade adaptation functioning normally, but degraded voluntary saccadic adaptation [@Alahyane2008].

@Panouillères2013 examined the cerebellar substrates of adaptive shortening by looking for disassociations between reactive and volitional saccades among patients with damage to, or impaired input to (because of Wallenberg Syndrome), regions of the cerebellum. In a study of patients with cerebellar lesions, @Panouillères2013 found that while damage to the medio-posterior cerebellum does not deferentially impair either reactive or volitional saccades, damage to supero-anterior regions showed specific deficits in the adaptation of voluntary saccades[@Panouillères201].

[Not so clear, take care extrapolating reactive to voluntary] As with the comparison of saccadic augmentation and reduction, the relationship between the two types of saccades is far from clear, even in the case of the cerebellar localization. Despite @Alahyane2008 finding a double disassociation between medial and lateral cerebellar regions, others have found evidence that both types of saccades activate hemispheric lobules [@Gerardin2012]. Prudence is called for when comparing, or attempting to extrapolate between reactive saccadic adaptation, and, for example, voluntary scanning saccades.

FIXME: above is my terrible attempt to clarify the ambiguity involved in using reactive saccadic adaptation with neglect patients, who exhibit pathological scanning eye movements.

### Colliculus drives eye movements, but is outside adaptive mechanisms

[SC is central to saccades] Because saccades can be generated by electrical stimulation of the superior colliculus [@Fitzgibbon1986], and because it is well connected with both the oculomotor vermis and areas of the cortex which seem related to eye movement control and saccadic adaptation [@Johnston2008], the superior colliculus is a possible locus of saccadic adaptation, or at minimum, a contributing player in a network of structures performing the adaptation.

[but adapted parameter is post SC] If the adaptable "gain" parameter is applied to saccadic movement execution after being generated in the superior colliculus, then the relationship between this generated signal and the actual saccadic magnitude should be modifiable with saccadic adaptation. While early research involving stimulation of the DLSC of the superior colliculus of monkeys failed to find any modulating effect of saccade adaptation [@Fitzgibbon1986;@Melis1996], some researchers have found indications of a connection [@Edelman2002]. @Edelman2002 found that they could modify electrically evoked movements with saccadic adaptation if the electrical stimuli were very low current (near threshold), and even then, only when the velocity of electrically evoked saccades was similar to the visually guided saccades in the adaptation. Nevertheless, the their success provides strong evidence that voluntary saccades, at least, occur by adapting a parameter which is post-superior colliculus. Further support comes from cell recordings of primate collicular motor cells, which show a remarkable consistency in the face of behavioural saccadic adaptation [@Frens1997], further supporting the notion that parametric adaptation occurring downstream of the colliculus.

### Cortical areas either contribute, or adapt in parallel

[Unlikely contributor to adaptation]While there is considerable evidence that reactive saccades are driven dominantly by the superior colliculus, and volitional saccades, a cortical-dominant system [@Schiller1987;@Johnston2008;@Schraa-Tam2009;@Müri2008], saccadic adaptation of the parameters of those saccades seems to occur at a common stage [@Hopp2002]. This finding is problematic for the notion that cortical areas may contribute to saccadic adaptation, as the time-course for reactive saccadic adaptation seems to rule out very much cortical involvement [@Hopp2002]. Nevertheless, there are some suggestions that the cortex may play a part.

[parallel pathways hypothesis] @Melis1996 used a target-jump paradigm to adaptively modify electrically stimulated saccades (superior colliculus). After adaptation, only a partial transfer to visually elicited saccades -indicating that some portion of the system was not affected by the electrically stimulated saccades. The authors postulate that both direct projections from both the frontal eye fields and superior colliculus to a brainstem saccadic generator. These parallel pathways are combined to produce parametric adaptation, and adaptation of only a single pathway would be expected to produce only partial adaptation of natural saccades.

FIXME: Above two paragraphs conflict. Clarify.

[Monkey/Human & 2-pathways aside] This theory also indicates caution where generalizations from monkey research are required. The weightings of the two parallel pathways are not likely to be completely identical between species, and with the enlarged cortical areas of the human brain, it seems probable that the relative contributions of the cortex may also have been changed [@Fuchs1996;@Frens1994]. This is supported by the fact that time course of adaptation is shorter in humans [@Deubel1986; Frens1994] relative to monkeys [@Fuchs1996; Straube1997; Scudder1998] . As with any field of research, it's debatable how much of the monkey-human differences are due to unique neural functionality, and how much is due simply to experimental design differences required by the different capabilities of the subjects.

FIXME: above paragraph unnecessary.

### Locus of adaptation

Examining the particularities of saccadic adaptation and the neural functionality of saccades are deeply intertwined. Most of the behavioural and psychophysical evidence discussed in earlier sections here provide clues about where in the perception and action systems the adaptation may be occurring. More specifically, though, we are able to glean an estimate of the earliest stages of vision, and the latest stages of perception and action systems that are involved in saccadic adaptation, providing a rough outline of the functional anatomy.

[Adaptation common between volitional and adaptive] @Hopp2002 behaviourally adapted participants to either voluntary or reactive saccades and found that to the extent that participants retained the adaptation to the trained type, it transferred equally to the other. This provides evidence supporting the notion that, despite the two types of *saccades* involving different functional systems, *adaptation* is probably happening at a shared point, like the brainstem or cerebellum, rather than, for example, a cortical area. This result was supported in a more recent replication that found transfer between the two types of adapted saccades, but no mutual transfer to or from adapted memory-guided saccades [saccades to remembered target locations; @Hopp2010].

[or, at least, overlapping] @Alahyane2007 also examined the mutual transfer of reactive and voluntary saccades, and while they also found bidirectional transfer of adaptation, it was much less than 100% in the specific case of transfer from reactive to voluntary saccades. This asymmetrical transfer lead them to suggest that adaptation of the two types is at least partially distinct, perhaps involving common brainstem and different, or overlapping, cerebellar regions [@Alahyane2007].

FIXME: Info about learning models would go here if necissary. See info in scratch space below.

## Scratch Space

Learning models ------------------------------------------------- @Fujita2005 developed a model of feed-forward associative motor learning which works by associating the primary motor command with the corrective motor command directly. The implication is that the motor centre and learning device share the same place-encoded information, the motor centre issues a learning signal and motor command as one signal, from the same unit, and the learning signal issued with a corrective command has a heterosynaptic interaction with the previous primary command.

* tDCS suggests cerebellum may produce short-term modifications of forward models, with the neocortex storing longer-lasting memories [@Galea2011]. TODO: This^ paper is important for model updating generally.

error signals influence dynamics (peak velocity) [@Straube1995], and what does this tell us about saccadic regulation [@Ethier2008]

Prediction based error signal [@Wong2012]

Both the Cerebellum [@Noda1991, @Lewis1992] and the superior colliculus [@Sparks1990; @Guitton1991] are known to be critical for the generation of goal-directed saccades.

[Neither random perturbations nor static targets are good controls for SA]@Desmurget2000 conducted a PET study with participants in three conditions of saccadic adaptation (reactive saccades). The conditions involved target perturbations occurring either systematically (adaptation condition), randomly, or not at all (static target). They examined three potential loci for the effects of saccadic adaptation (i.e., a contrast of the adaptation condition and the random condition), the frontal-eye fields, the superior colliculus, and the oculomotor vermis area of the cerebellum. They found evidence that the cerebellum structure was activated deferentially during adaptation, but neither of the other two structures. Interestingly, when comparing the saccade metrics of the static and random conditions, they also found effects of single-trials. So it's possible that some of the adaptive mechanisms were equally engaged in the random condition as with the adaptive condition. The frontal eye fields still did not become active when comparing adaptation with the static condition, however, and this is consistent with what other researchers have postulated, that frontal eye fields are more specialized for voluntary, self-generated saccades rather than the reactive saccades used in this experiment [@Deubel1995 pp3538]. The authors also did not find superior colliculus activity in either contrast, but are more cautious in interpreting this null result, because of the lack of PET sensitivity in the deep structure, and a conflicting result by @Paus1995. Perhaps the most intriguing finding, the single-trial effects, display an insurmountable problem in the literature. No-perturbation controls are insufficient because they, in addition to lacking adaptation, also lack the corrective saccades and provide a generally much more predictable environment for the participant, while random-perturbation controls seem to actually be impacting adaptive systems -albeit in a way that, over the long term, produces no systematic changes. As a result, neither control is very effective.

Transfer of eye movements to head movements in humans [@Kroller1996] compared with monkeys [@Phillips1997;@Fuchs1996].

Bilateral Frontal-eye field activation during oculomotor tasks [@Paus1993!].

Snippets from Hopp2004: @Hopp2004: a slide in post-saccadic eye position has been induced by exponen- tial motion of a full-field stimulus at the end of a saccade (e.g., Optican and Miles, 1985; Deubel, 1991; Kapoula et al., 1987).

@Hopp2004: SA can be induced by the wearing of specialized prisms (Henson, 1978) or anisotropic glasses (Lemij and Collewijn, 1991; Albano and Marrero, 1995; Erkelens et al., 1989; Oohira et al., 1991; Bush et al., 1994; Averbuch-Heller et al., 1999).

@Hopp2004: By analogy with such SC “motor fields”, Frens and van Opstal (1997) named the spatial property of saccadic adaptation an “adaptation field.”

@Hopp2004: In both monkeys and humans, a spot target that moves across a stationary background, whether a random dot pattern, a combination of squares and circles, or a colour photo, in- duces robust adaptation if the spot target alone undergoes an adaptation step (Deubel, 1995a; Ditterich et al., 1999; Robinson et al., 2000). Furthermore, in humans, adapta- tion to a spot target with or without a background present is statistically the same (Ditterich et al., 1999)

@Hopp2004: the focus of attention itself does not seem to shift with saccadic adaptation. In the experi- ments of Ditterich et al. (2000a)...