Aalto University
School of Science

Effect of linearly increasing galvanic vestibular stimulation on balance

Special Assignment in Human Neuroscience and Technology

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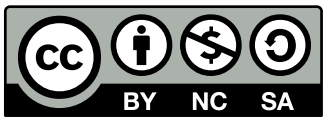
2024



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Title Effect of linearly increasing galvanic vestibular stimulation on balance — Special Assignment in Human Neuroscience and Technology

Degree programme Life Science Technologies

Major Human Neuroscience and Technology

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Date 7 September 2023 **Number of pages** 31 **Language** English

Abstract

Galvanic vestibular stimulation is a non-invasive technique, where the vestibular system is stimulated with electric current through electrodes placed on the mastoids behind the ears. This current activates the otoliths and semicircular canals in the inner ears, which causes postural and balance responses such as swaying. Different current waveforms can be used for the stimulation, but previous research lacks the study of linearly increasing current and its effects on human balance.

This special assignment studies the balance responses of galvanic vestibular stimulation where the current intensity increases linearly, by analysing the centre of pressure responses. The data for this analysis has been acquired previously for another ongoing study. This assignment studied whether the current intensity affects the response intensity. The assignment also studied if having eyes closed during the stimulation affects the balance response. Linear mixed-effects models were used for the analysis. The findings show that galvanic vestibular stimulation, where current increases linearly, continuously shifts the centre of pressure of subjects' balance laterally until stimulation is stopped. This effect is stronger when the subject has their eyes closed during the stimulation. When the current intensity and the rate of change are larger, the effect is also stronger. This study addressed the research gap of the effects of galvanic vestibular stimulation with linearly increasing current on human balance.

Keywords GVS, balance, linear mixed-effects model, centre of pressure, electrical stimulation

Contents

Symbols and abbreviations

Symbols

A	ampere

Abbreviations

AIC	Akaike information criterion
CoP	centre of pressure
CoPx	centre of pressure, x-direction
CoPy	centre of pressure, y-direction
GVS	galvanic vestibular stimulation
LMM	linear mixed-effects model
M	mean
SD	standard deviation
SE	standard error
tES	transcranial electrical stimulation

1 Introduction

The human balance system controls the postural reactions to keep the body's centre of gravity in equilibrium. Information from the vestibular, visual and somatosensory systems determine this centre of gravity (Olchowik et al. 2015). The balance system can encounter many different complications, such as vestibular hypofunction, which refers to an underactive state of the vestibular system (Starkov et al. 2021), among others that can be missed or misdiagnosed, or that lack a definitive cure. However, one promising method in aiding in the diagnosis, assessment and possibly even treatment of these issues is through galvanic vestibular stimulation.

Galvanic vestibular stimulation (GVS) is a non-invasive stimulation technique, where current is applied to the vestibular system through the mastoid parts of the temporal bones behind the ears. This stimulation can cause different kinds of involuntary balance and postural responses, as well as oculomotor responses. The postural responses can include body sway, dizziness and perception of illusory movements (Fitzpatrick & Day 2004). GVS is a relatively new stimulation method, and its activation areas and potential clinical applications are still under research, however it has been known to be useful especially in diagnostics (Dlugaiczyk et al. 2019). Research has shown that GVS could possibly help with for example, bilateral vestibulopathy (Wuehr et al. 2016), motion sickness (Rizzo-Sierra et al. 2014) and Parkinson's disease (Lee et al. 2021), and it has been studied for use in the entertainment field, particularly in the context of video games (Byrne et al. 2016).

Various studies have used different waveforms of current, such as steps and sinusoids to study the human balance and GVS (Dlugaiczyk et al. 2019). However, the effects of GVS with linearly increasing current on human balance have not been studied extensively.

In this special assignment, I will study existing balance response data from GVS experiments conducted in Ilkka Laakso's research group at Aalto University. I will specifically study the linear 5-second current ramp-up period at the beginning of the stimulation, and what kinds of balance responses it causes. To support this analysis, I will create a linear mixed-effects model to predict the slope of the balance response based on the stimulation current used. In the second chapter, the basic principles of the vestibular system and galvanic vestibular stimulation will be explained. In the chapter I will also go through the previous experiments and explain how the source data used in this special assignment was acquired. In the third chapter I will describe the data more thoroughly and go through the methods and results of my analysis. In the last chapter I will discuss the conclusions, implications and limitations of the results of this special assignment.

2 Background

2.1 Vestibular system

The vestibular system is located in the inner ear, and consists of two otolith organs and three semicircular canals. The otoliths, the utricle and saccule, sense mainly linear acceleration of the head, such as when sitting in an accelerating car or standing in a moving elevator. The semicircular canals sense angular acceleration in different directions (Day & Fitzpatrick 2005).

The three rotational directions of the human head or other objects can move towards are yaw, pitch, and roll dimensions (i.e. a turning-like motion, nodding-like motion, and tilting-like motion, respectively) (Jantunen et al. 2016).

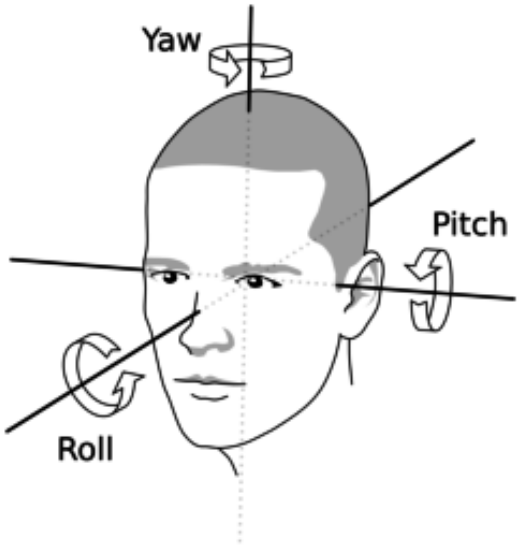

Figure 1: The three rotational movement directions of the head, yaw, pitch and roll. Image from Jantunen et al. (2016).

2.2 Galvanic vestibular stimulation

Galvanic vestibular stimulation (GVS) is a non-invasive stimulation technique, where electric current is applied through electrodes to the mastoid parts of the temporal bones behind the ears. This stimulates the vestibular system, which can evoke balance responses such as swaying and leaning, and perception of illusory head motion. This illusory head motion is interpreted as real movement that is a threat to balance, and results in postural overcorrections. According to the most recent findings, GVS activates all vestibular organs, although there have been different views about the subject (Dlugaiczyk et al. 2019). GVS works by polarising hair cells in the vestibular system and surrounding nerves. When the head is in a normal upright and forward-facing position, anodal GVS produces a large roll component and a yaw component.

The resultant vector is therefore backward and slightly upward (Figure 2), which indicates a signal of head roll towards the cathodal side. This is what causes the virtual head motion, and it leads to a corrective tilt towards the anode (Fitzpatrick & Day 2004).

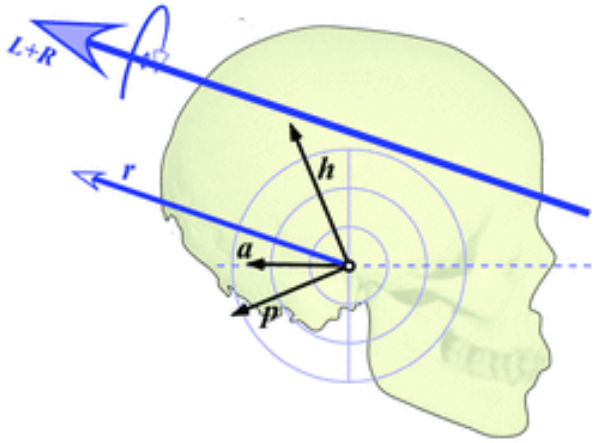

Figure 2: The vector L+R shows the direction of the net rotational vector of the balance response. The curved arrow around the vector shows the direction of the sway according to the right-hand rule. Modified from St George & Fitzpatrick (2011).

GVS has a lot of potential for use in clinical applications. It can especially be useful in diagnostic and rehabilitative applications when studying vestibular dysfunction (Dlugaiczyk et al. 2019). The electric currents for GVS are usually steps, sinusoids, trains of short pulses or band-limited noise (Dlugaiczyk et al. 2019). The usual balance response to current steps for example is a tilt towards the anodal side. However, this motion stops in a couple of seconds, and the body is left in a static tilt (Figure 3) (Fitzpatrick & Day 2004).

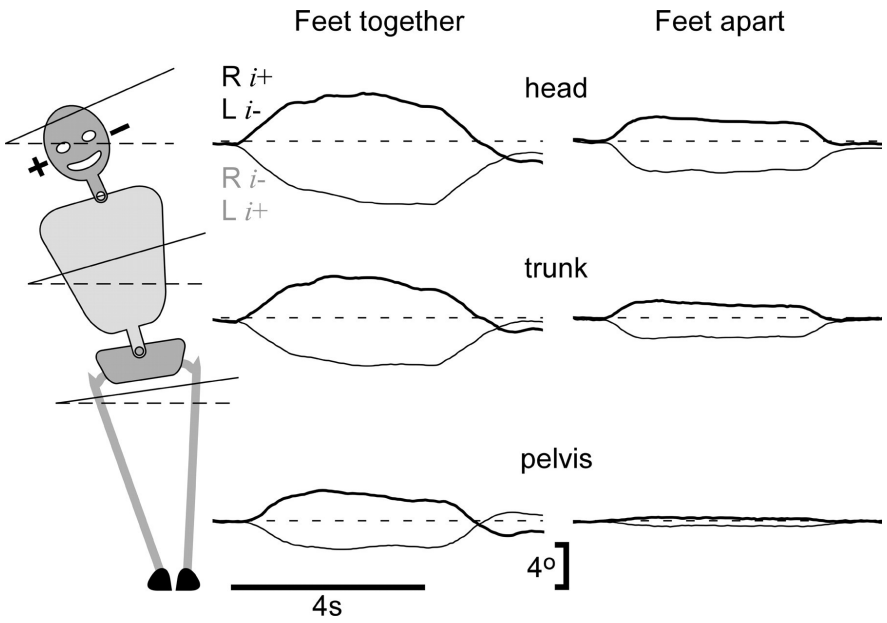

Figure 3: Alignment of the body after GVS with a four-second current pulse. After a couple of seconds of stimulation, the tilt of the body reaches a steady level. After the stimulation stops, the body straightens quickly back to a normal position. The pattern is the same, but attenuated when the feet are apart. Figure from Fitzpatrick & Day (2004).

GVS with linearly growing current has not been extensively explored in prior studies. Many studies have used linearly increasing ramp-up periods at the beginning and end of the actual stimulation to reduce unnatural head rotation and tingling sensations, that can be caused by current steps (Dlugaiczyk et al. 2019), but response measurements are often performed after the ramp-up period, and the responses during the ramp-up period are left unanalysed.

To the best of my knowledge, at the time of writing there have been no previous studies, where GVS with linearly increasing current intensity and its effects on balance have been researched. Therefore, this special assignment aims to study what happens to the human balance during GVS where the current intensity increases linearly.

2.3 Original experiments

Janita Nissi, a member of Ilkka Laakso's research group at Aalto University, had performed experiments for an ongoing study, where the subjects stood on a balance board during galvanic vestibular stimulation. At the beginning of each trial, there were two current steps and a 5-second ramp-up period before the actual stimulation. During this ramp-up period, the current intensity increased linearly from 0 until reaching the maximum current of either 750, 1000, or 1500 μA, depending on the trial. Figure 4 depicts an example of this stimulation signal. This time period during the current ramp-up will be the subject of this special assignment.

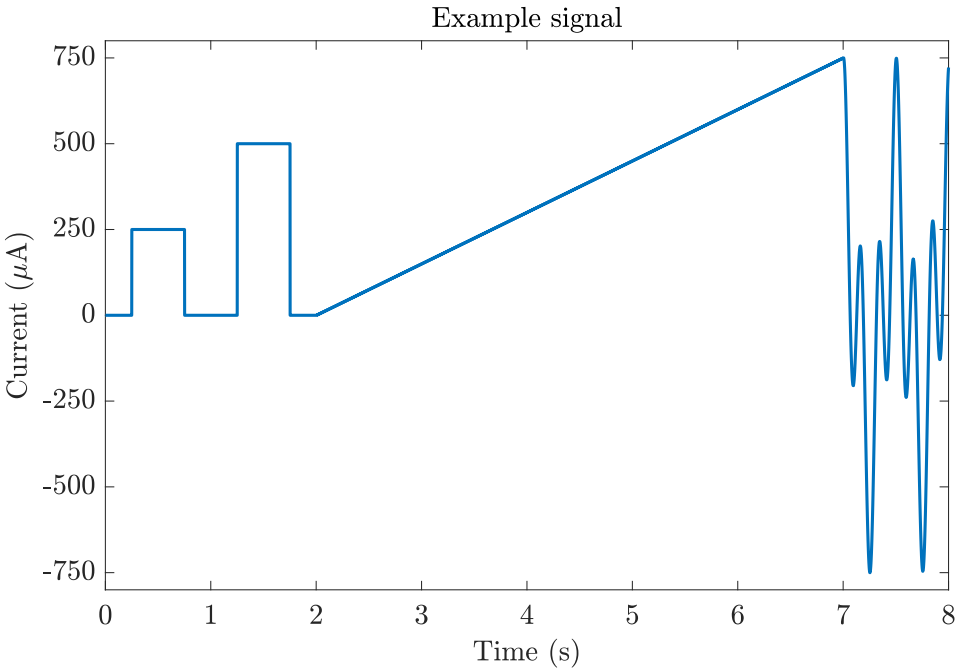

Figure 4: An example of the stimulation signal, where the maximum current is 750 μA. The ramp-up period can be seen between the 2-second mark and the 7-second mark.

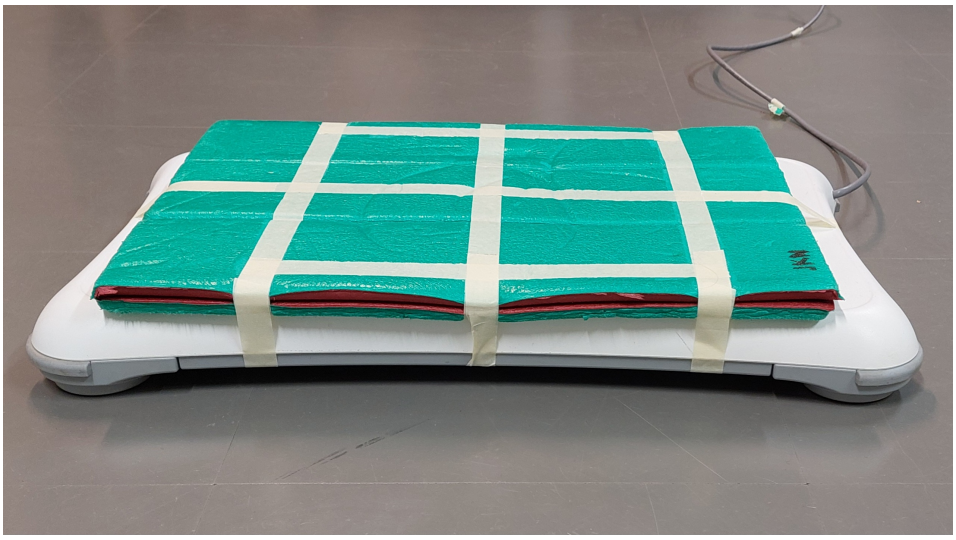

Figure 5: The Nintendo Wii balance board used to measure the centre of pressure during the experiment. The foam mat on top of the board reduced the somatosensory inputs from the soles of the feet to make balancing on the board a bit more difficult.

Ten healthy subjects, three females and seven males, aged between 23 and 63 years (M = 33.7 years) participated in the study. In the experiments the subjects stood feet together, without shoes, on a balance board (Figure 5) which recorded their centre of pressure (CoP) responses during the stimulation. On top of the board, there was also a thin foam mat to reduce the amount of somatosensory information from the soles of the feet to make balancing on the board a bit more difficult. The maximum current achieved at the end of the ramp-up period varied between trials, but each ramp-up period lasted 5 seconds. Also, the fact whether a subject's eyes were open or closed during the experiment varied between trials. The experiment was double-blinded and randomised. Electric current was applied through electrodes placed on the mastoids behind the ears during the trials. This stimulation was applied with a Neuroelectrics Starstim 20 transcranial electrical stimulation (tES) stimulator, and stimulation current was measured with a Pico Technology PicoScope 2406B oscilloscope. Balance responses were measured with a modified Nintendo Wii balance board. The Nintendo Wii balance board is a motion-sensing video game controller, which has been previously proven to be a valid tool for assessing balance, in addition to being portable and inexpensive compared to a laboratory-grade force platform (Clark et al. 2010). The width of the board is 0.430 metres. The board measured and recorded pressure with sensors from its four corners: right front, left front, right back and left back corner. In the equation below, the variables 'rightFront', 'rightBack' etc. refer to these four sensors. The centre of pressure was then calculated for each time point. In this study we are mainly interested in CoP in the x-direction, as GVS mainly causes postural responses towards the ear with the anode, i.e. laterally (Fitzpatrick & Day 2004). We will also verify this by investigating whether any balance responses can be observed in the y-direction.

$$CoPx = \frac{0.430\ m}{2} \frac{(rightFront + rightBack) - (leftFront + leftBack)}{rightFront + rightBack + leftFront + leftBack}$$

Plotting the CoPx of each subject shows this postural response as a continuous change in CoPx. An example of one subject's CoPx during the ramp-up period can be seen in Figure 6. Based on the visual inspection of the graphs, it seems that CoPx decreases gradually over time, i.e. moves towards the left. The kind of linearly increasing current used in this experiment, has not been previously used in GVS research, therefore we have no prior knowledge of what kind of balance responses it should evoke.

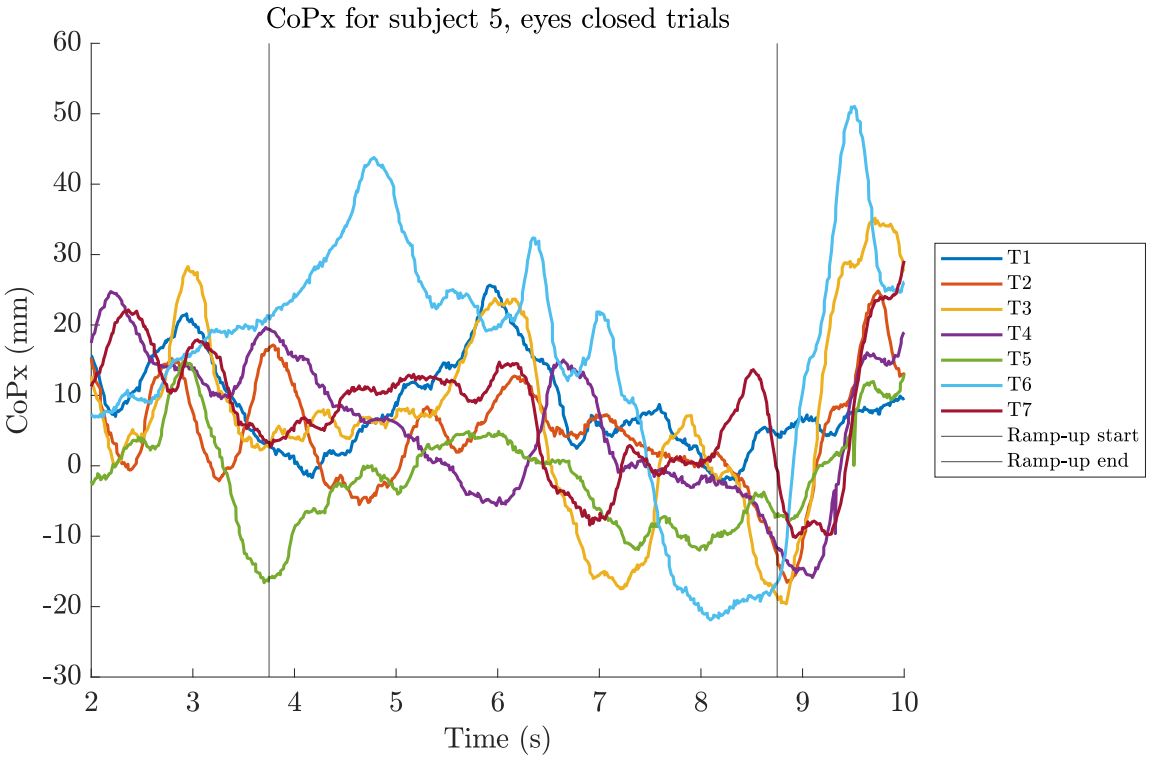

Figure 6: CoPx of subject 5 during the ramp-up period. After synchronising the signals, the ramp-up period is roughly between 3.75 and 8.75 seconds. During this time period, the CoPx seems to decrease.

Based on this initial visual analysis, my objective was to investigate the potential decrease in CoPx attributed to the stimulation. If it is indeed decreasing, I want to determine the relationship between the stimulation and the subsequent CoPx response. Does a higher current or a faster rate of change result in a steeper CoPx decline? Can we identify a minimum current that would cause a significant balance response? If a larger maximum current does cause a steeper decline in CoPx, is there a significant difference in the change of CoPx between subjects? Are certain individuals more susceptible to the effects of the stimulation? Lastly, I will study whether having eyes open or closed influences the degree of steepness in the CoPx slope.

3 Materials and methods

3.1 Data

All data analysis and plotting for this special assignment have been performed utilising MATLAB (MATLAB 2023), a widely used software environment for scientific computing and data analysis.

For this analysis, the lateral centre of pressure data, i.e. CoPx data, from 14 trials and 10 subjects was used. Of the 14 trials, seven were with eyes closed and seven with eyes open, both including one sham trial where no ramp-up period occurred. In each non-sham trial, the ramp-up current started from 0 A and ended in either 750, 1000 or 1500 μA, depending on the trial. Therefore the corresponding rates of change are 150, 200 and 300 μA/s respectively. Each maximum current was used in the experiment four times, two with eyes closed and two with eyes open. The sham trials will be considered as trials in which no ramp-up period takes place, meaning a maximum current of 0 A.

In total, 14 trials and 10 subjects add up to 140 samples. Subject 11 had four individual trials which had been halted before the ramp-up period, which were omitted from this study. These four samples will not be used in the analysis, therefore in the end 136 data samples were used. Before the analysis, the accompanying oscilloscope data was synchronised with MATLAB function 'alignsignals'. The delays given by the function for each signal were used to synchronise the CoPx data. For the analysis, only CoPx data from the 5-second ramp-up period was used.

3.2 Data analysis

Based on visual inspection, the CoPx data seems to demonstrate a downward trend, i.e. the CoPx shifts towards the negative values continuously as a result of the stimulation. This means that GVS causes the subjects to tilt in one direction, to the left in this case. The investigation of this fact began with fitting a linear model to the ramp-up data for each of the 136 CoPx samples and looking at the models' slopes. The linear models were fitted with MATLAB function 'fitlm'. An example of the fitted model can be seen in Figure 7 for subject 7. Going forward, these linear model slopes will only be referred to as slopes, and they are an integral part of this study.

The majority (106 of 136) of the slopes are negative (Figure 8) (M = -2.1440, SD = 3.2983), which indicates that the linearly increasing current causes a noticeable shift in balance in almost all of the samples. The shift seems to continue throughout the ramp-up period.

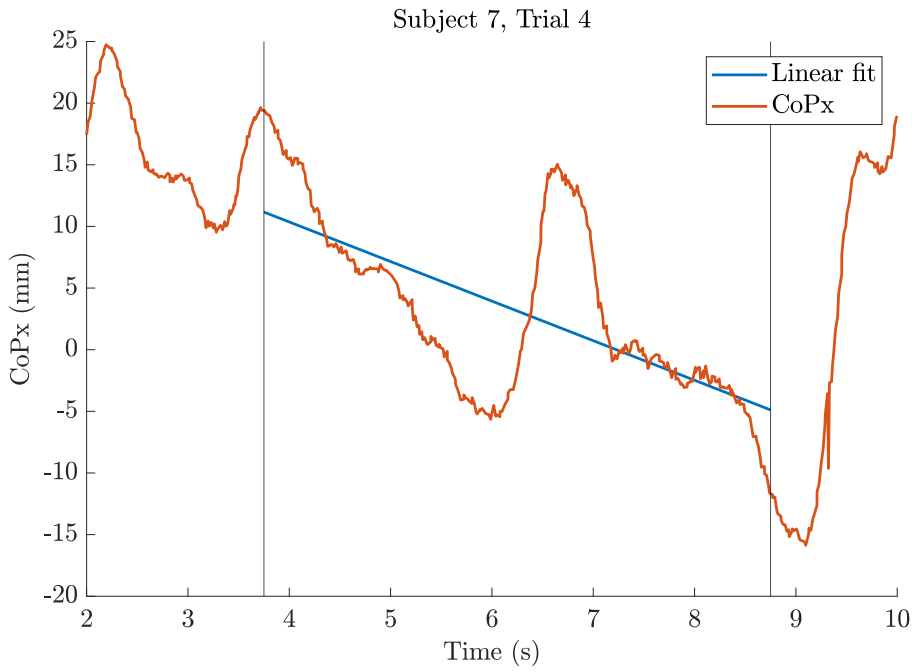

Figure 7: Linear fit to CoPx during the ramp-up period for subject 7, trial 4. The plot clearly shows the continuous shift in balance that occurs during the stimulation.

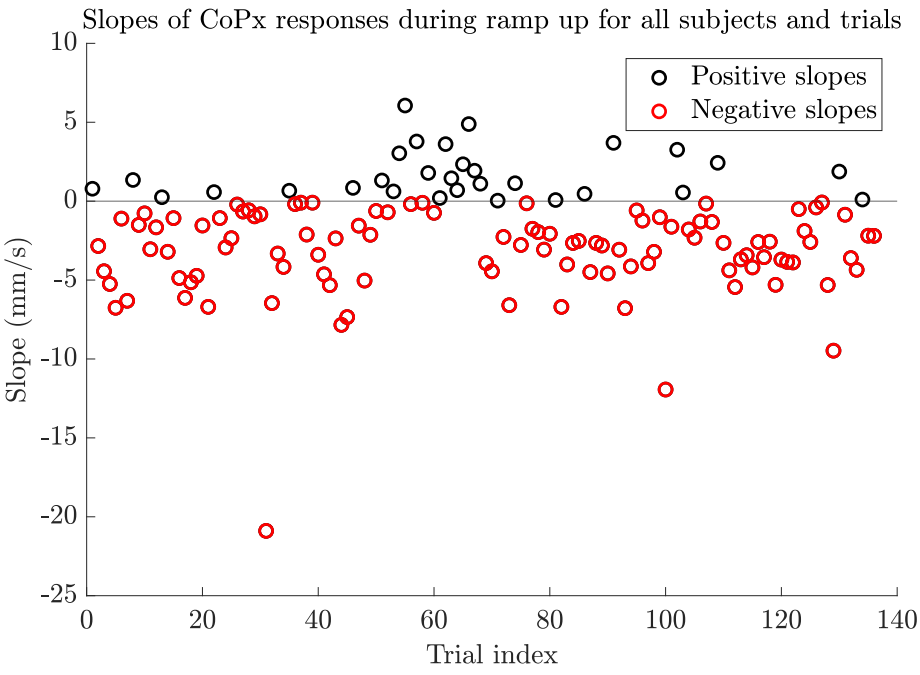

Figure 8: Magnitude of the slope of each linear fit of CoPx signals. 106 out of 136 slopes are negative.

There is some variation in the slopes between subjects (Figure 9). Some subjects responded less significantly to the stimulation and had slopes closer to zero. Subject 2 seems to be an outlier in the data, as their slopes are mostly positive, which indicates a tilt to the right, rather than left like all the other subjects. The reason for this remains unknown, since the stimulation polarity was consistent across all trials. This matter will be explored more in the discussion section.

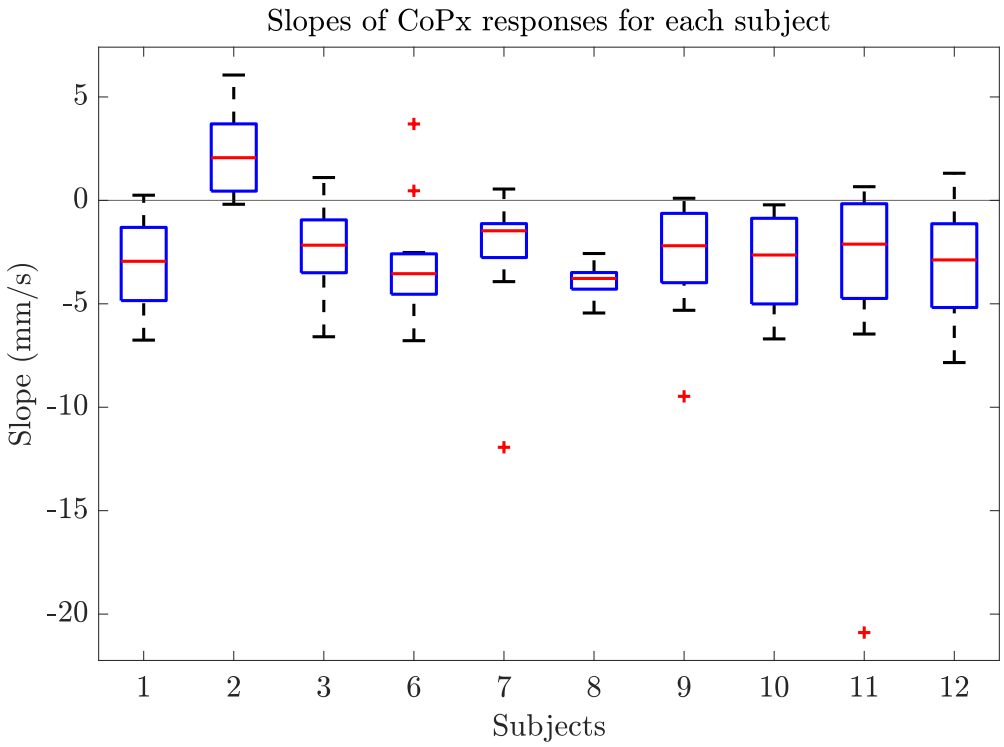

Figure 9: Boxplots show the minimum, maximum, median, and the first and third quartiles for the slopes of each subject. This plot contains slopes of CoPx data from all trials, except the sham trials. Most of the boxes lie almost entirely on the negative side.

Then the trials where subjects had their eyes closed were compared to the trials where the eyes were open. This is because the loss of visual input should cause stronger postural responses (Fitzpatrick & Day 2004), and therefore the slopes should be more negative. A comparison of these scenarios can be seen in Figure 10. The average balance response is stronger, i.e. more negative, when the eyes are closed (M = -2.4763, SD = 3.5237) compared to when they are open (M = -1.2324, SD = 2.2555).

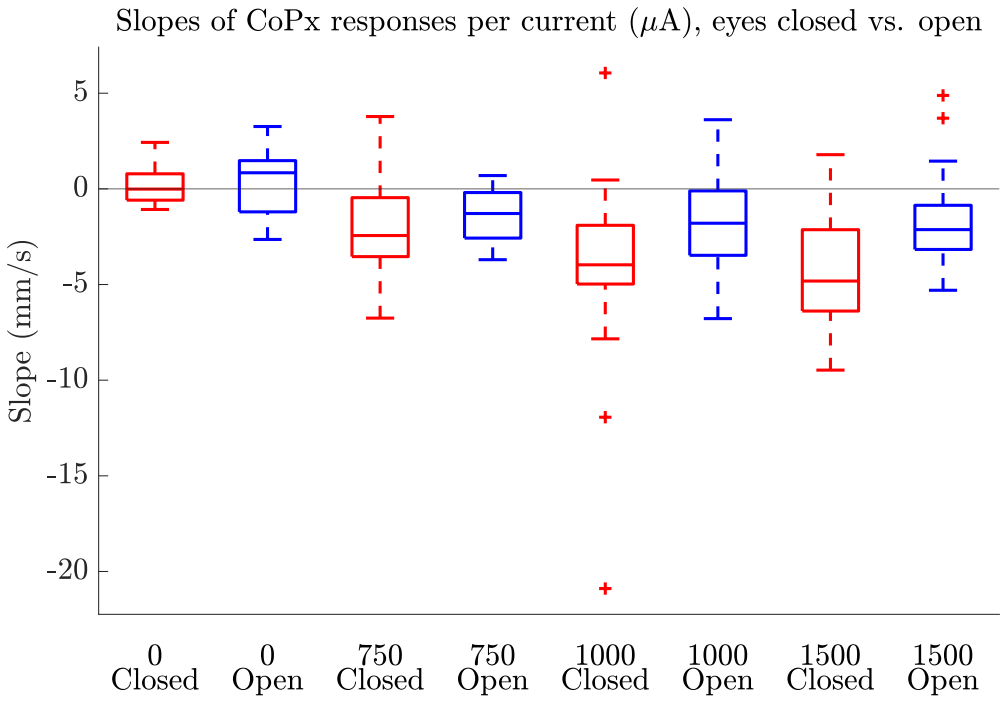

Figure 10: Boxplots show the minimum, maximum, median, and the first and third quartiles for the slopes when the eyes are closed vs. open for each maximum current. For each current, there is a stronger balance response when the eyes are closed compared to when they are open.

To confirm that we are not missing any important information by only studying the CoPx signals, I performed the same data analysis to the CoPy signals and studied the slopes of the linear models. The results can be seen in Figures 11, 12 and 13. CoPy slopes are much closer to zero than CoPx slopes, because the CoPy signals mostly consist of natural swaying. By comparing these figures to the corresponding ones of CoPx slopes (Figures 8, 9 and 10), and referring to previous research about the effects of GVS (e.g. Fitzpatrick & Day (2004)), I came to the conclusion that in this experiment GVS did not cause balance responses in the y-direction, and I will not study the CoPy signals further.

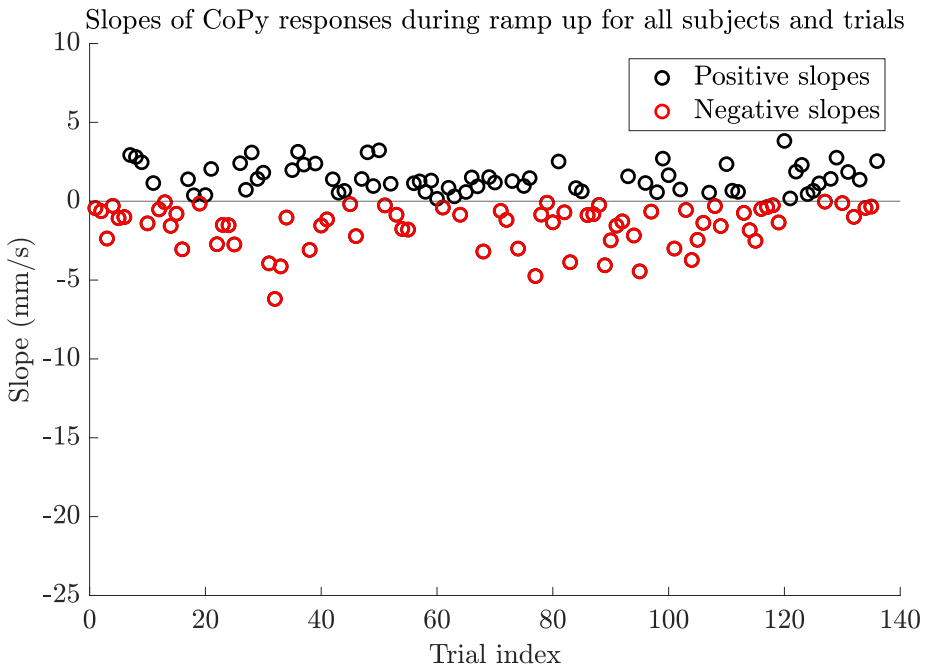

Figure 11: Magnitude of the slope of each linear fit of CoPy signals. 71 of 136 slopes are negative, a significantly lower count compared to the CoPx slopes.

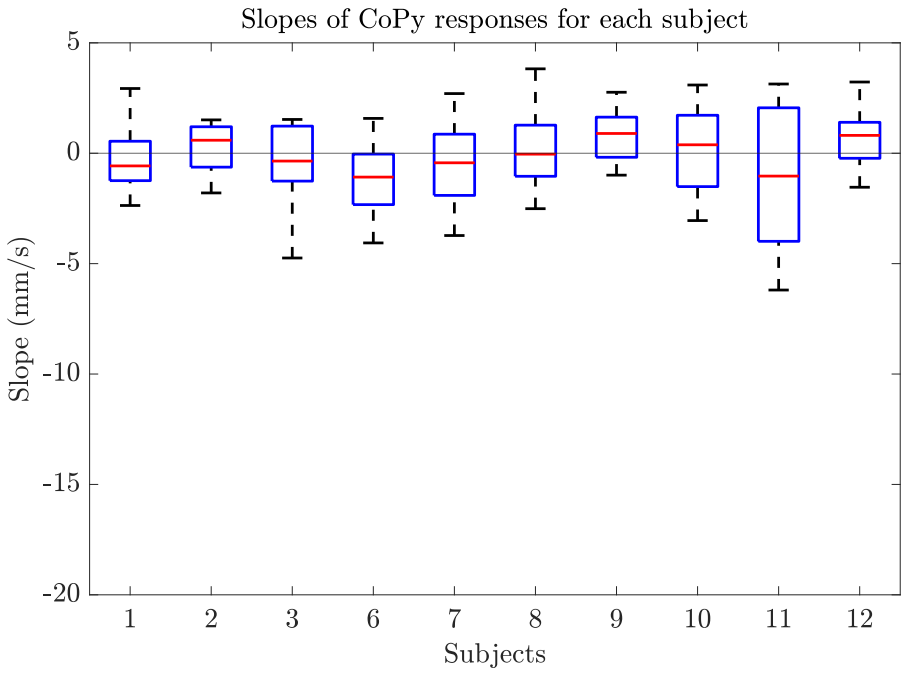

Figure 12: Boxplots show the minimum, maximum, median, and the first and third quartiles for the slopes when the eyes are closed vs. open for each maximum current. This plot contains slopes of CoPy data from all trials, except the sham trials. Most of the boxes lie close to zero.

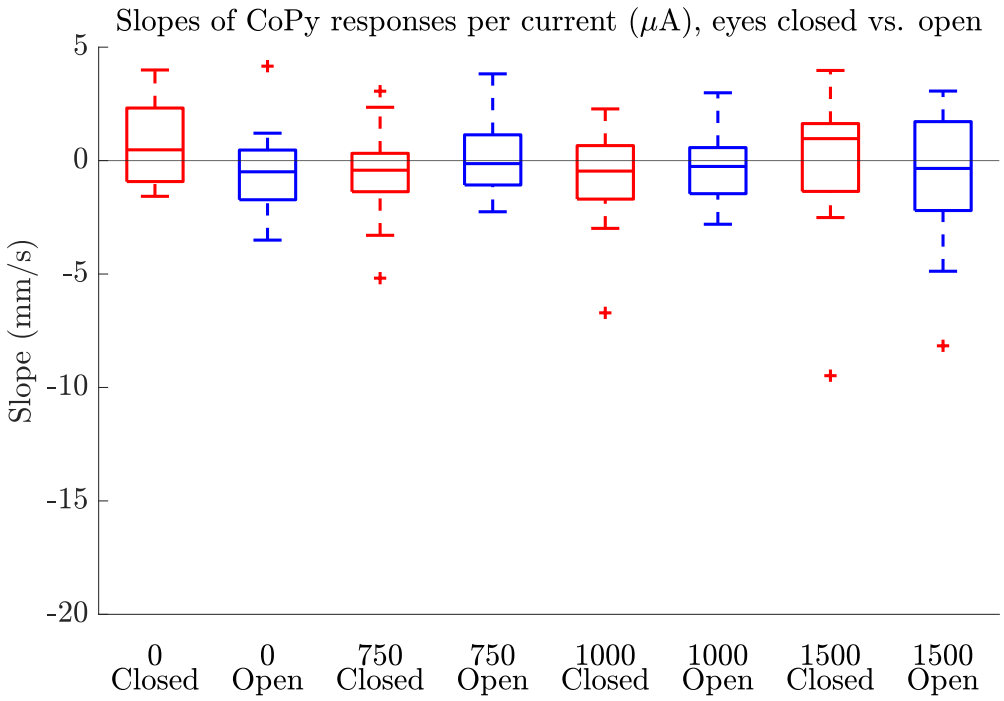

Figure 13: Boxplots show the minimum, maximum, median, and the first and third quartiles for the slopes when the eyes are closed vs. open for each maximum current. There is no significant difference between the eyes closed and open slopes in the y-direction.

I then compared the effects of different currents on the CoPx slopes. Trials in which the eyes were closed were separated from ones with eyes open. All of the trials with the same maximum current were combined for both scenarios. The CoPx data was then averaged over time for each current and eye-status, and a linear model was fitted to the data. The results can be seen in Figure 14. Based on the graphs, it seems that the slope does become steeper as the maximum current increases. It also seems that the current has a stronger effect on the slope when the subject's eyes are closed.

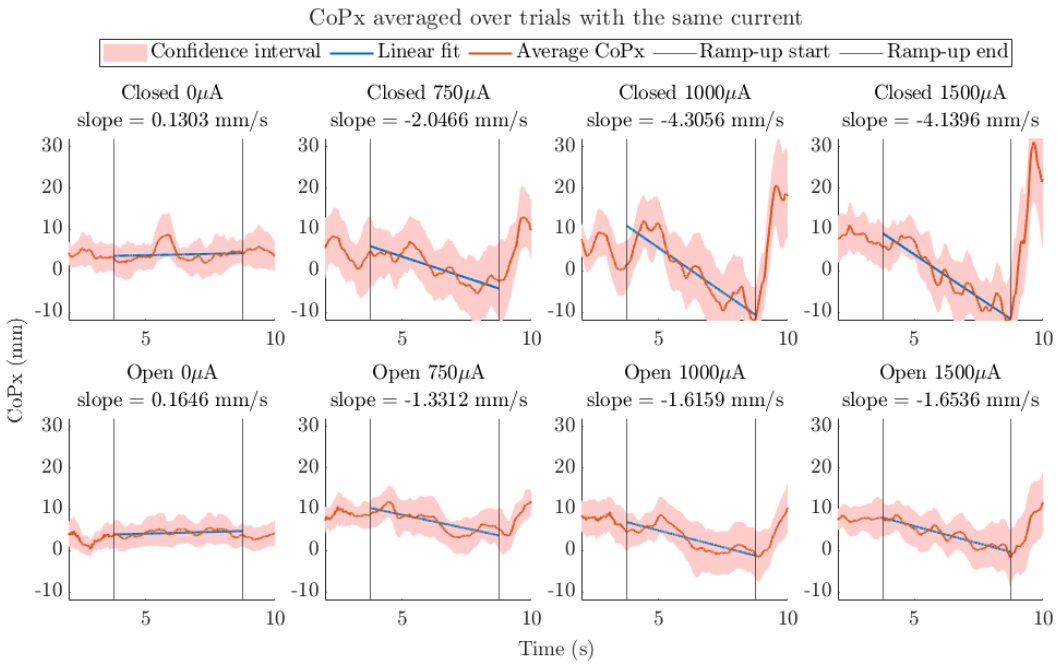

Figure 14: Linear regression fit to average CoPx for each maximum current with a 95% confidence interval. The slopes are more negative the larger the maximum current and the rate of change are. The effect is stronger when the subject's eyes are closed.

Lastly I wanted to investigate if there exists a point on the current graph, i.e. a minimum current, where significant balance responses could be found. I studied this by fitting linear models to CoPx signals of different ramp-up period lengths. For example, in the 750 μA maximum current, the ramp reaches 100 μA at about 0.5 seconds after onset (see Figure 4). I would only use this short snippet of the CoPx signal to fit a linear model to it and studying the resulting slopes. For the different minimum currents I studied the mean and standard deviation of all slopes, and if the mean of the slopes was significantly negative which would indicate that GVS causes significant balance responses at this minimum current. The results of these tests are in Table 1.

Table 1: Table of the different minimum currents and the means and standard deviations of the slopes (mm/s), as well as the p-value of the one-sample t-test. 450 μA is the smallest current that causes significant balance responses.

Minimum current (μA)	Mean	Standard deviation	p-value
100	2.59	25.4	0.237
200	1.94	14.68	0.126
300	1.13	8.89	0.139
350	0.156	7.55	0.810
400	-0.668	6.61	0.241
450	-1.39	5.79	0.0059

I found that 450 μA is the minimum current for linearly increasing GVS, that causes significant balance responses. The limitation of studying these very short periods of time is that CoPx fluctuates also due to natural swaying, which can be seen as large standard deviation values, and larger trends caused by GVS can mainly be seen on a longer time scale, than a couple of seconds.

In the next chapter I will create a linear mixed-effects model to test the significance of the observed negative slopes, variations between subjects and the impact of closed eyes.

3.3 Linear mixed-effects model

A linear mixed-effects model (LMM) is a statistical model with fixed effects and random effects. Fixed effects are parameters associated with an entire population, and random effects are parameters associated with individual parts of the experiment drawn at random from a population. Mixed-effects models can be used to describe relationships between a response variable and grouped covariates in data. With random effects, these models can flexibly represent the covariance structure caused by the data grouping (*Linear Mixed-Effects Models: Basic Concepts and Examples* 2000).

The MATLAB function 'fitlme' was used to create a linear mixed-effects model to analyse the relationship between the slope of the CoPx and maximum current. The significance of the variation between the subjects, as well as the significance of the difference in slopes slopes between having eyes open and closed, were also under investigation. LMMs are useful in this case, because they account for the fact that CoPx samples from the same subject are more similar than samples from other subjects. All of the following models use a diagonal covariance pattern and dummy variables created with effects coding.

I created the optimal LMM by starting with the most bare-bones model, and adding variables one by one, while testing their significance. First the relationship between the CoPx slope and maximum current was examined, without factoring in the eye-status

or variation between subjects. As a fixed effect, i.e. the predictor variable, I used the maximum current, without including any random effects.

$$Model\ 0 : Slope \sim Current$$

Table 2: Model 0: Estimated fixed effects coefficients, their standard errors, t-values and p-values for the t-test. The t-statistic is for testing the null hypothesis that the coefficient is equal to zero.

Explanatory Variable	Estimate	SE	t-value	p-value
Current	-0.00227	0.000256	-8.87	3.34e-15

From Table 2 we can see that the estimate for the current is negative and the p-value is very small, which indicates that there is a significant negative correlation between the maximum current of the ramp-up period and the CoPx slope. The Akaike Information Criterion (AIC) of this model is 699.69. Next I added the intercept variable (1) to test whether the intercepts of the models, i.e. the 0 A slopes differ based on the current.

$$Model\ 1 : Slope \sim 1 + Current$$

Table 3: Model 1: Estimated fixed effects coefficients, their standard errors, t-values and p-values for the t-test. The t-statistic is for testing the null hypothesis that the coefficient is equal to zero.

Explanatory Variable	Estimate	SE	t-value	p-value
Intercept	-0.130	0.591	-0.220	0.826
Current	-0.00216	0.000565	-3.83	0.000199

The p-value of the intercept (p = 0.826) shows that the variable is not significant, and the AIC of this model, which is 701.65, also indicates. For the next model, I added a random effect grouped by subject to capture the variability between individual people. Here we assume that the intercept might vary by subject.

$$Model\ 2 : Slope \sim Current + (1 \mid Subject)$$

Table 4: Model 2: Estimated fixed effects coefficients, their standard errors, t-values and p-values for the t-test, as well as the standard deviation (SD) of the random effects and their confidence limits. The t-statistic is for testing the null hypothesis that the coefficient is equal to zero.

Explanatory Variable	Estimate	SE	t-value	p-value
Current	-0.00224	0.000361	-6.20	6.43e-9
Random effect	Grouped by	SD	Lower limit	Upper limit
Intercept	Subject	1.28	0.699	2.33

Table 4 shows the results of Model 2. To test whether the random effect coefficient was significant I compared Model 0 and 2 with the MATLAB function 'compare', which uses the theoretical likelihood ratio test. Model 2 was significantly better ($p < 0.001$) and its AIC was lower (690.01) than the AIC of Model 0. This would mean that there are significant differences in the intercepts between subjects, which means that sham slopes vary between subjects. This result seemed odd, since most of the 0 A slopes were near zero and shouldn't have any significant differences between them since there is no stimulation occurring. Therefore I researched this more by repeating the model creation without data from subject 2, who we suspected to be an outlier earlier in the study (see Figure 9). The results now showed that the random effect was not significant. I also tested removing other subjects instead of subject 2, but every time subject 2 was included in the model, the random effect was significant. Therefore we can conclude that the random effect of the intercept grouped by subject is only significant, because subject 2 is an outlier in the data. I decided not to remove subject 2 from the data set or the random effect from the model, as then we might lose some important information and the model would not fit as well. For the next model I added current as a random effect grouped by subject, to see if the current affects subjects differently.

$$Model\ 3 : Slope \sim Current + (1 + Current \mid Subject)$$

Table 5: Model 3: Estimated fixed effects coefficients, their standard errors, t-values and p-values for the t-test, as well as the standard deviation (SD) of the random effects and their confidence limits. The t-statistic is for testing the null hypothesis that the coefficient is equal to zero.

Explanatory Variable	Estimate	SE	t-value	p-value
Current	-0.00230	0.000465	-4.92	2.45e-6
Random effect	Grouped by	SD	Lower limit	Upper limit
Intercept	Subject	0.298	5.28e-6	16800
Current	Subject	0.00125	0.000528	0.00297

I then again compared Model 2 and 3 to test whether current as a random effect was significant. The results showed that Model 3 was not significantly better (p = 0.122, AIC = 689.62) than Model 2, which means that the current does not affect the slope differently for different subjects. Next I wanted to study the effect of having eyes closed during the experiments. I created two models and added 'Eyes' as a fixed effect to both, but with Model 5 having possible interaction with current. I kept the random effects the same as in Model 2.

$$Model\ 4 : Slope \sim Current + Eyes + (1 \mid Subject)$$

Table 6: Model 4: Estimated fixed effects coefficients, their standard errors, t-values and p-values for the t-test, as well as the standard deviation (SD) of the random effects and their confidence limits. The t-statistic is for testing the null hypothesis that the coefficient is equal to zero.

Explanatory Variable	Estimate	SE	t-value	p-value
Current	-0.00223	0.000350	-6.37	2.79e-9
Eyes_Closed	-0.823	0.235	-3.51	0.000610
Random effect	Grouped by	SD	Lower limit	Upper limit
Intercept	Subject	1.27	0.702	2.28

$$Model\ 5 : Slope \sim Current * Eyes + (1 \mid Subject)$$

Table 7: Model 5: Estimated fixed effects coefficients, their standard errors, t-values and p-values for the t-test, as well as the standard deviation (SD) of the random effects and their confidence limits. The t-statistic is for testing the null hypothesis that the coefficient is equal to zero.

Explanatory Variable	Estimate	SE	t-value	p-value
Current	-0.00221	0.000348	-6.35	3.09e-9
Eyes_Closed	0.0444	0.509	0.0872	0.931
Current:Eyes_Closed	-0.000930	0.000486	-1.91	0.0579
Random effect	Grouped by	SD	Lower limit	Upper limit
Intercept	Subject	1.28	0.713	2.29

The comparison of Model 4 to Model 2 shows that the eye-status does affect the slope significantly (p < 0.001), but comparing Model 4 and 5 seems to suggest that the interaction between the current and eyes is not significant (p = 0.058), but the AIC of Model 4 is 680.23 and Model 5 is 678.62 which means that Model 5 fits the data better than Model 4. Model 5 also fits our assumptions of the study better, since the intercepts of the models should be the same for eyes closed and eyes open trials, and

the model for eyes closed should have a steeper decline than the model for eyes open. For these reasons we will be using Model 5 going forward, as it fits our purposes better even though it wasn't significantly better than Model 4. Then I modified Model 5 and added eyes as a random effect grouped by subject, but comparing this new model to Model 5 showed that the effect was not significant (p = 0.559, AIC = 680.28), which means that the effect of having eyes closed or open is not significantly different for subjects. The rest of the results for Model 6 can be seen in Table 8.

$$Model\ 6 : Slope \sim Current * Eyes + (1 + Eyes|\ Subject)$$

Table 8: Model 6: Estimated fixed effects coefficients, their standard errors, t-values and p-values for the t-test, as well as the standard deviation (SD) of the random effects and their confidence limits. The t-statistic is for testing the null hypothesis that the coefficient is equal to zero.

Explanatory Variable	Estimate	SE	t-value	p-value
Current	-0.00221	0.000345	-6.40	2.45e-9
Eyes_Closed	0.0296	0.519	0.0571	0.955
Current:Eyes_Closed	-0.000925	0.000480	-1.92	0.0564
Random effect	**Grouped by**	**SD**	**Lower limit**	**Upper limit**
Intercept	Subject	1.27	0.712	2.27
Eyes_Closed	Subject	0.404	0.0570	2.86

Lastly I tried out a model which contains all of the variables I have used so far, Model 7. The AIC of this model is 679.2 and it is not significantly better than Model 6 (p = 0.0792, AIC = 680.28). No other model outperformed Model 5, therefore we can conclude that out of all the models, Model 5 fits our data best.

$$Model\ 7 : Slope \sim Current * Eyes + (1 + Current + Eyes|Subject)$$

Table 9: Model 7: Estimated fixed effects coefficients, their standard errors, t-values and p-values for the t-test, as well as the standard deviation (SD) of the random effects and their confidence limits. The t-statistic is for testing the null hypothesis that the coefficient is equal to zero.

Explanatory Variable	Estimate	SE	t-value	p-value
Current	-0.00225	0.000456	-4.94	2.27e-6
Eyes_Closed	-0.00894	0.513	-0.0174	0.986
Current:Eyes_Closed	-0.000895	0.000471	-1.90	0.0595
Random effect	**Grouped by**	**SD**	**Lower limit**	**Upper limit**
Intercept	Subject	0.369	0.000806	169
Current	Subject	0.00123	0.000562	0.00271
Eyes_Closed	Subject	0.455	0.0921	2.24

Next I used Model 5 to predict slopes for each subject for each of the currents used in the original experiments (0, 750, 1000 and 1500 μA). The model predictions are shown in Figure 15. In the figure we can see the most notable results of this study. A large maximum current or current rate of change causes a more negative CoPx slope. When the eyes are closed, this effect is even stronger, except for a 0 A where the slope is near zero in both scenarios.

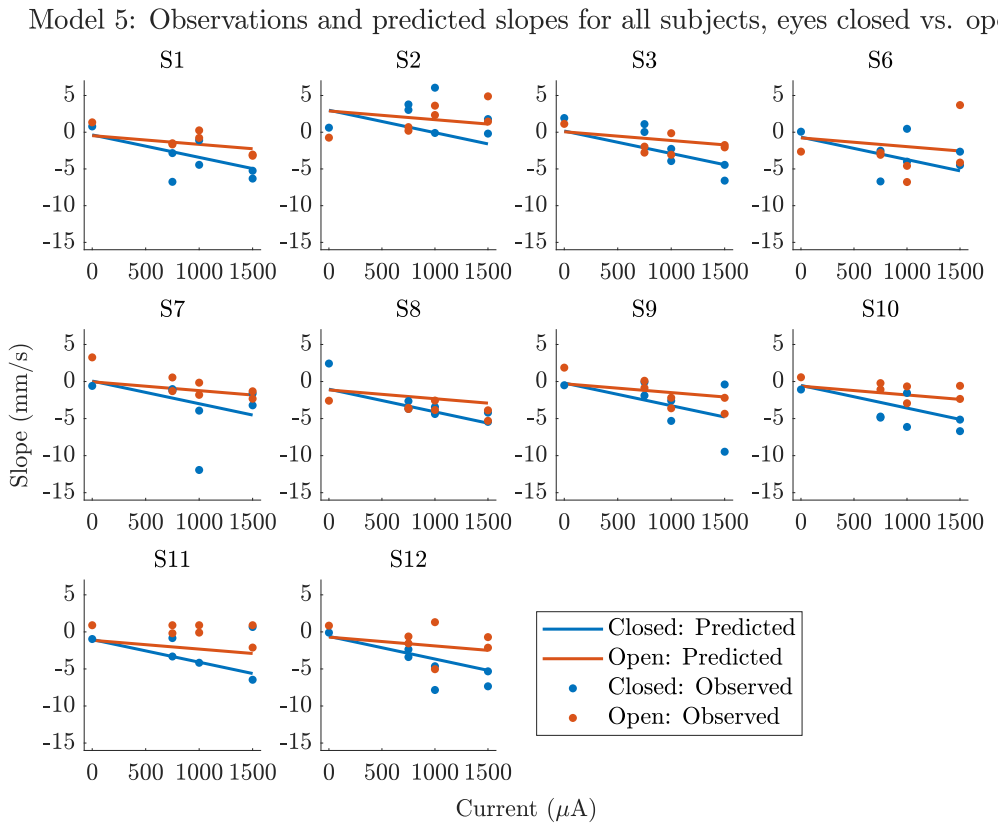

Figure 15: Model 5: Predictions and observations of the linear mixed-effects model for each subject.

Lastly, I wanted to study if any carryover effects could be seen in the trials appearing later in the randomised order. Theoretically, these trials would have more negative slopes due to the carryover effects, in addition to the effect of the current. Therefore I created a model similar to Model 5, but added Trial as a fixed effect with possible interaction with current. Trial is the order number of a trial for a specific subject ranging from 1 to 14, with 1 being the first trial of a subject and 14 being the last. Hypothetically, trials with larger order numbers would have steeper slopes compared to trials with the same current, but smaller order numbers.

$$Model\ 8 : Slope \sim Current * Trial * Eyes + (1|\ Subject) + (1 + Current|\ Trial)$$

Table 10: Model 8: Estimated fixed effects coefficients, their standard errors, t-values and p-values for the t-test, as well as the standard deviation (SD) of the random effects and their confidence limits. The t-statistic is for testing the null hypothesis that the coefficient is equal to zero.

Explanatory Variable	Estimate	SE	t-value	p-value
Current	-0.00249	0.000541	-4.59	1.02e-5
Eyes_Closed	0.201	1.19	0.169	0.866
Trial	-0.00867	0.0716	-0.121	0.904
Current:Eyes_Closed	-0.00117	0.00120	-0.980	0.329
Current:Trial	3.82e-5	8.72e-5	0.438	0.662
Eyes_Closed:Trial	-0.0246	0.151	-0.163	0.871
Current:Eyes_Closed:Trial	3.32e-5	0.000147	0.226	0.822
Random effect	**Grouped by**	**SD**	**Lower limit**	**Upper limit**
Intercept	Subject	1.29	0.719	2.30
Intercept	Trial	0.000500	3.66e-313	6.83e+305
Current	Trial	0.000820	2.51e-199	2.68e+192

To compare the effect of Trial, Trial's interaction with Current, Trial's interaction with Eyes and the interaction between all three of them, I created different models excluding these individual variables one by one and again used the theoretical likelihood ratio test to test each variable's significance. I will not report the coefficients of these models, but the p-values of the tests are in Table 11 below, which are the same as the p-values of the coefficients in Table 10.

Table 11: Table containing the results of the theoretical likelihood ratio test comparing Model 8 to models where the specified variable has been excluded to test its significance.

Explanatory Variable	p-value
Trial	0.904
Eyes:Trial	0.871
Current:Trial	0.662
Current:Eyes:Trial	0.822
(1 | Trial)	≈ 1
(Current | Trial)	≈ 1

None of the variables including the Trial is significant. This means that the trial order number does not affect the slope on its own, or together with the current. Therefore there aren't any significant carryover effects in this study.

4 Discussion

This special assignment aimed to find what kind balance responses galvanic vestibular stimulation with linearly increasing current causes. I studied balance data of a 5-second ramp-up period from a previous GVS experiment, where current intensity started from 0 A and ended in 750, 1000 or 1500 μA. I found that GVS with linearly increasing current significantly and continuously shifts the centre of pressure of subjects' balance laterally towards the anode. I found that 450 μA is the minimum current where significant balance responses can be found. The balance response is stronger when the subject has their eyes closed during the stimulation. When the ramp-up current is larger, the effect of having eyes closed is also stronger. As for subjects, there was significant variation only in the intercepts of the models, i.e. in sham trial slopes, which could be due to natural swaying. A linear mixed-effects model for predicting the slopes based on the maximum current and eye-status was created. No significant carryover effects were found in the experiment.

Previously GVS has been known to cause lateral shifting in balance, which stops after a couple seconds leaving the body in a static tilt, when using current steps as stimulation (see Figure 3). However I found that for linearly increasing current this effect continues until the current ramp stops.

The significance of this special assignment lies in the exploration of a topic that has received limited attention in previous studies. To the best of my knowledge this is the first extensive investigation into the effects of GVS with linearly increasing current on human balance. This study contributes to the existing body of knowledge about GVS by addressing this research gap. While the results of this special assignment are not surprising in nature, they do provide insight into GVS and give an opportunity for further research. In the future this study could be continued with ramp-up and ramp-down periods of different durations and intensities to further study the relationship between the maximum current and the slope of the CoPx.

Despite the new result gained from this study, there are some limitations that may have affected these findings. Firstly, the sample size used in the prior study, where the data for this special assignment came from, was relatively small, consisting of only 10 subjects. The limited number of participants may restrict the generalisability of the results. Secondly, the lack of prior studies about stimulation with this specific waveform makes it difficult to compare the results to any previous empirical findings. It also limits the extent to which this study could explore the responses of linear GVS. Lastly, the four stimulation currents studied in this special assignment all had different rates of change, which is most likely the reason the CoPx responses are different for each maximum current. Future studies should also research this question further with different rates of change and maximum currents.

There were a few noteworthy outliers in the data, most notably subject 2. Their slopes are more positive than others', and they seem to exhibit a growing trend rather

than a declining one, when current intensity grows. This means that they tilted to the right rather than left. A scenario where this would happen, would be GVS where the electrodes are the other way around, but that is not the case here, as the correct placement of electrodes was checked multiple times. A more plausible reason is that the subject has a good balance and was able to resist the effects of GVS, and the resulting slopes are more due to random natural swaying, rather than stimulation. Natural swaying can also explain some of the non-zero slopes observed in the sham trials.

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