$$\mathbb{S}^{q-1} := \{\boldsymbol{y} \in \mathbb{R}^q : \|\boldsymbol{y}\| = 1\},$$

For $\boldsymbol{y} \in \mathbb{S}^{q-1}$, the probability density function of von Mises-Fisher distribution (vMF) is defined as

$$f_{vMF}(\boldsymbol{y} : \boldsymbol{\zeta}, \kappa) = C_q(\kappa) \exp\left(\kappa \boldsymbol{\zeta}^T \boldsymbol{y}\right)$$

for a concentration parameter $\kappa \geq 0$ and mean direction $\boldsymbol{\zeta} \in \mathbb{S}^{q-1}$. Here, $C_q(\kappa)$ is a normalization constant defined as

$$C_q(\kappa) = \frac{\kappa^{q/2-1}}{(2\pi)^{q/2} I_{q/2-1}(\kappa)},$$

where $I_\nu(\cdot)$ is the modified Bessel function of the first kind at order ν.

Here, the mean direction parameter ζ is restricted on a unit sphere, so we can consider the following reparametrization to alleviate this. If we let $\boldsymbol{\theta} = \kappa\boldsymbol{\zeta}$ for $\kappa > 0$, then $\kappa = \|\boldsymbol{\theta}\|$ with $\boldsymbol{\theta} \in \mathbb{R}^q$ and we have a reparametrized vMF distribution by a mean parameter $\boldsymbol{\theta} \in \mathbb{R}^q$:

$$f_{vMF}(\boldsymbol{y} : \boldsymbol{\theta}) = \exp\left(\boldsymbol{\theta}^T\boldsymbol{y} + \log C_q(\|\boldsymbol{\theta}\|)\right). \tag{1}$$

In addition, let us express the probability density function of a random vector following the exponential family as

$$f(\boldsymbol{y}|\boldsymbol{\theta}, \phi) = \exp\left(\frac{\boldsymbol{\theta}^T\boldsymbol{y} - b(\boldsymbol{\theta})}{a(\phi)} + c(\boldsymbol{y}, \phi)\right),$$

where $\boldsymbol{\theta}$ and ϕ are the natural and scale parameters, $b(\cdot)$ and $c(\cdot)$ are known functions related to different exponential responses. Then, the reparametrized

$$g\left(\mathbb{E}[\boldsymbol{y}_i|\boldsymbol{x}_i]\right) = \boldsymbol{\theta}_i = \boldsymbol{\mu} + \sum_{j=1}^{p} x_{ij}\boldsymbol{\beta}_j = \boldsymbol{\mu} + \boldsymbol{B}^T\boldsymbol{x}_i \quad \text{and } \boldsymbol{y}_i|\boldsymbol{x}_i \sim f_{vMF}(\cdot|\boldsymbol{\theta}_i),$$

- Constrained model : $\boldsymbol{\beta}_j \perp \boldsymbol{\mu}, \quad j = 1, \ldots, p$
- Unconstrained model : $\boldsymbol{\beta}_j \in \mathbb{R}^q, \quad j = 1, \ldots, p$

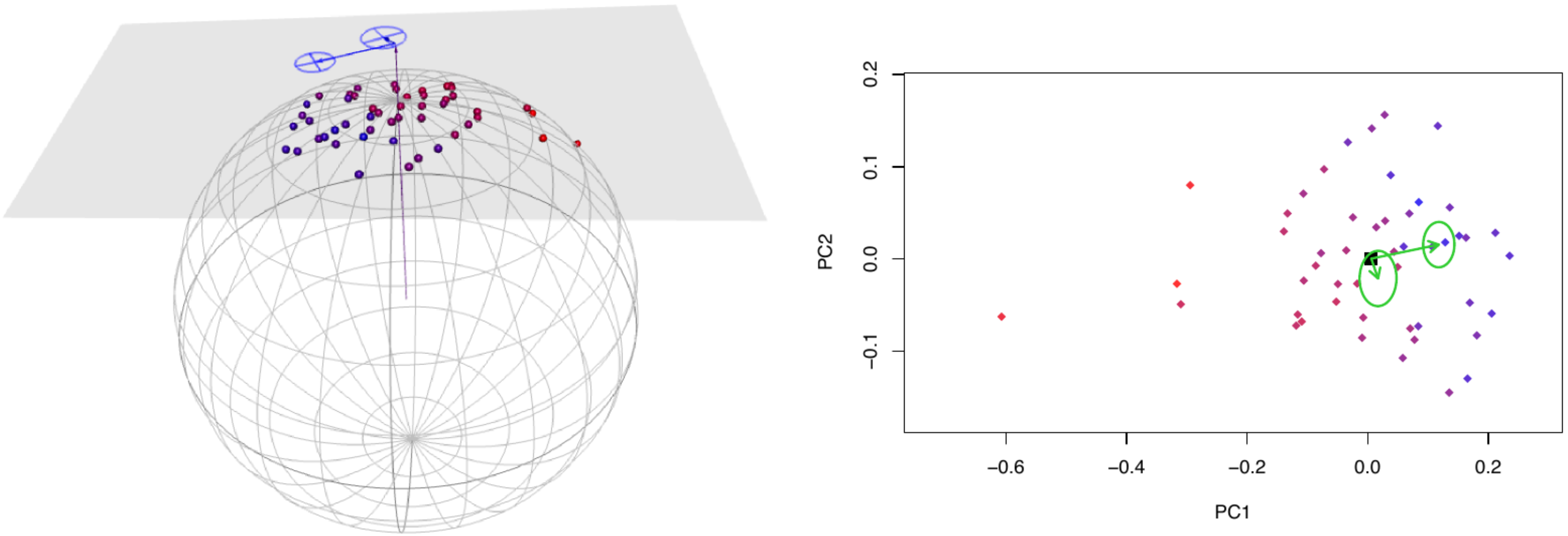


Figure 1: An example of regression model for vMF distributed spherical responses on $\mathbb{S}^2$. The red points indicates the spherical responses, the blue line the estimated regression coefficients, $\hat{\boldsymbol{\beta}}_1 = (4.80, -10.22, -0.20)^T$, $\hat{\boldsymbol{\beta}}_2 = (-1.71, -1.71, 0.08)^T$ with p-values $1.19 \cdot 10^{-12}$, and 0.1542, and the purple line the estimated mean direction $\hat{\boldsymbol{\mu}} = (2.41, 0.13, 48.69)^T$. For more visibility, the coefficients were normalized to have norm = 1.25.

- Global null hypothesis
$$H_0 : \boldsymbol{\beta}^* = \mathbf{0} \tag{6}$$

- Individual null hypothesis

$$H_{0j} : \boldsymbol{\beta}_j = 0, \tag{7}$$

  for $j = 1, \ldots, p$.

- Other hypotheses for mean or dispersion difference

  (1) Location difference: $H_A : \boldsymbol{\mu}^T \boldsymbol{\beta}_j = 0 \ \ \& \ \ \boldsymbol{\beta}_j \neq \mathbf{0}$

  (2) Dispersion difference: $H_A : \angle(\boldsymbol{\mu}, \boldsymbol{\beta}_j) = 0 \ \ \& \ \ \boldsymbol{\beta}_j \neq \mathbf{0}$

Lemma 1. *Under the assumptions (A1)–(A3), the normed score vector*

$$\boldsymbol{F}_n^{-T/2}\boldsymbol{s}_n(\boldsymbol{\beta}_0^*) \xrightarrow{D} N(\boldsymbol{0}, \boldsymbol{I}_{pq}) \quad \text{as } n \to \infty,$$

where $\boldsymbol{I}_{pq}$ is a pq-dimensional identity matrix.

Lemma 2. *Under the assumptions (A1)–(A3)*

$$\max_{\boldsymbol{\beta}^* \in N_n(\epsilon)} \|\boldsymbol{V}_n(\boldsymbol{\beta}^*) - \boldsymbol{I}_{pq}\| \xrightarrow{p} 0, \quad \forall \epsilon > 0,$$

where $\boldsymbol{V}_n(\boldsymbol{\beta}^*) := \boldsymbol{F}_n^{-1/2}\boldsymbol{F}_n(\boldsymbol{\beta}^*)\boldsymbol{F}_n^{-T/2}$.

Theorem 1. *Under the assumptions (A1)–(A3), the asymptotic normality of $\hat{\boldsymbol{\beta}}^*$ can be obtained as follows:*

$$\boldsymbol{F}_n^{T/2}(\hat{\boldsymbol{\beta}}^* - \boldsymbol{\beta}_0^*) \xrightarrow{d} N(\boldsymbol{0}, \boldsymbol{I}_{pq}).$$

3.2.1. Hypotheses

- Global null hypothesis

$$H_0 : \boldsymbol{\beta}^* = \boldsymbol{\beta}_0^* \tag{6}$$

- Individual null hypothesis

$$H_{0j} : \boldsymbol{\beta}_j = \boldsymbol{\beta}_{0j}, \tag{7}$$

for $j = 1, \ldots, p$.

For testing the null hypothesis (6), we introduce the Wald statistics as:

$$W_j := \hat{\boldsymbol{\beta}}_j^T \hat{\boldsymbol{F}}_{n,j}(\hat{\boldsymbol{\beta}}_j)\hat{\boldsymbol{\beta}}_j, \quad j = 1, \ldots, p, \tag{8}$$

where $\hat{\boldsymbol{F}}_{n,j}(\hat{\boldsymbol{\beta}}_j)$ is the empirical version of $\boldsymbol{F}_{n,j}(\boldsymbol{\beta}_{0j})$ evaluated at the maximum likelihood estimates, and $\boldsymbol{F}_{n,j}(\boldsymbol{\beta}_{0j})$ is the $q \times q$ dimensional submatrix consisting of the elements corresponding to the jth predictor in $\boldsymbol{F}_n(\boldsymbol{\beta}_0^*)$.

Theorem 2. *Under Assumptions (A1)–(A3), for $j = 1, \ldots, p$, if the null hypothesis $H_{0j} : \boldsymbol{\beta}_j = \mathbf{0}$ is true,*

$$W_j \xrightarrow{d} \chi^2(q)$$

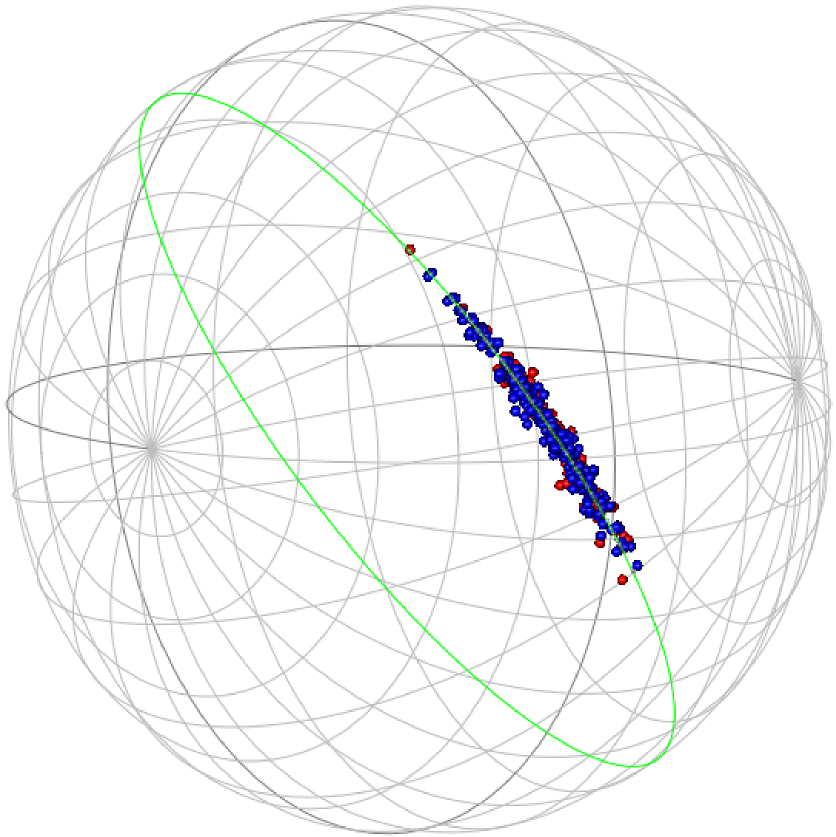
as $n \to \infty$, where $\chi^2(q)$ is the chi-squared distribution with q degrees of freedom.

Real data analysis: procedure

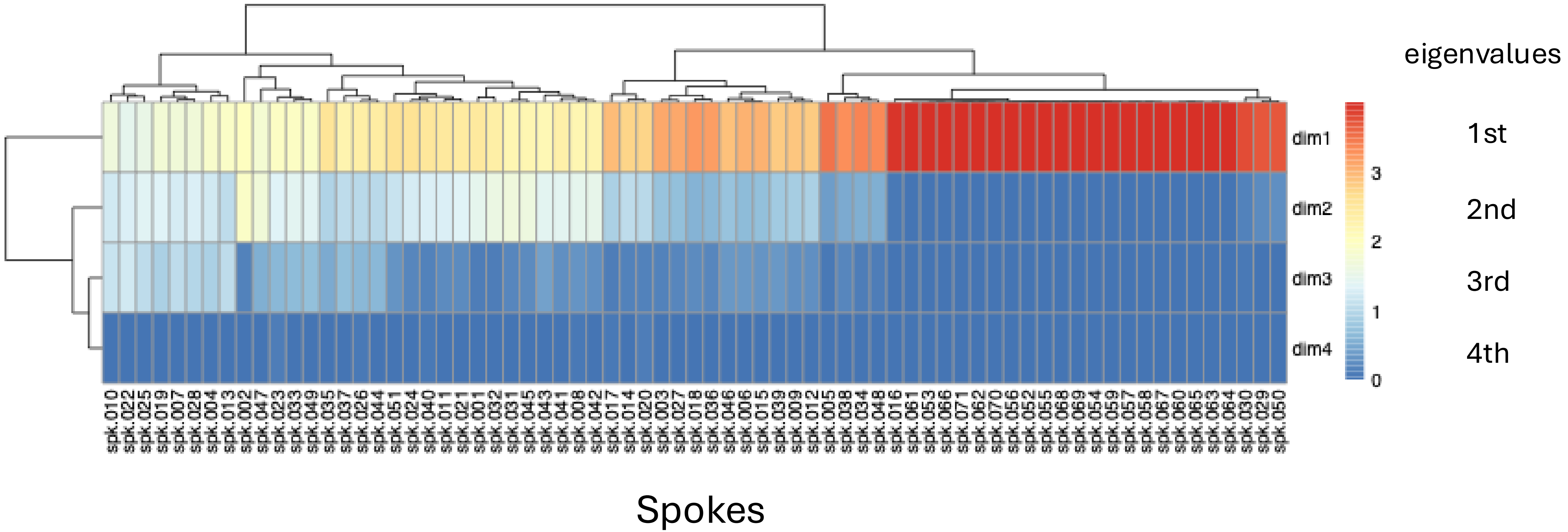
- Target responses = framesBasedOnParentsUnitQuaternion
  - Other choices: Spokes' directions, Connections' directions, …
- Covariate of interest = Parkinson disease (the presence or absence)
- The response variables are on S^3 but actually have a rank less than 3,
  >> so we use Principal Nested Sphere to get the responses projected onto S^2.
- We fit our two models separately to the responses on S^3 and to those projected onto S^2.
- Methods:
  - Orthogonally constrained sphereGLM
  - Unconstrained sphereGLM
- Our goal is to identify spokes associated with Parkinson's disease in terms of
  - (1) Location difference between two groups
  - (2) Dispersion difference between two groups

    (though it's questionable whether this has clinical significance)
- In (2) If there is a dispersion difference, compare the sample covariance matrix for each group in terms of total var.
- If a dispersion difference is found in (2), we'll compare the sample covariance for each group in terms of total variance
- For better visibility, we coded the covariates to be -0.1 for control and +0.1 for case to increase the size of estimates.

Principal Nested Sphere (PNS) : Example (spk26)

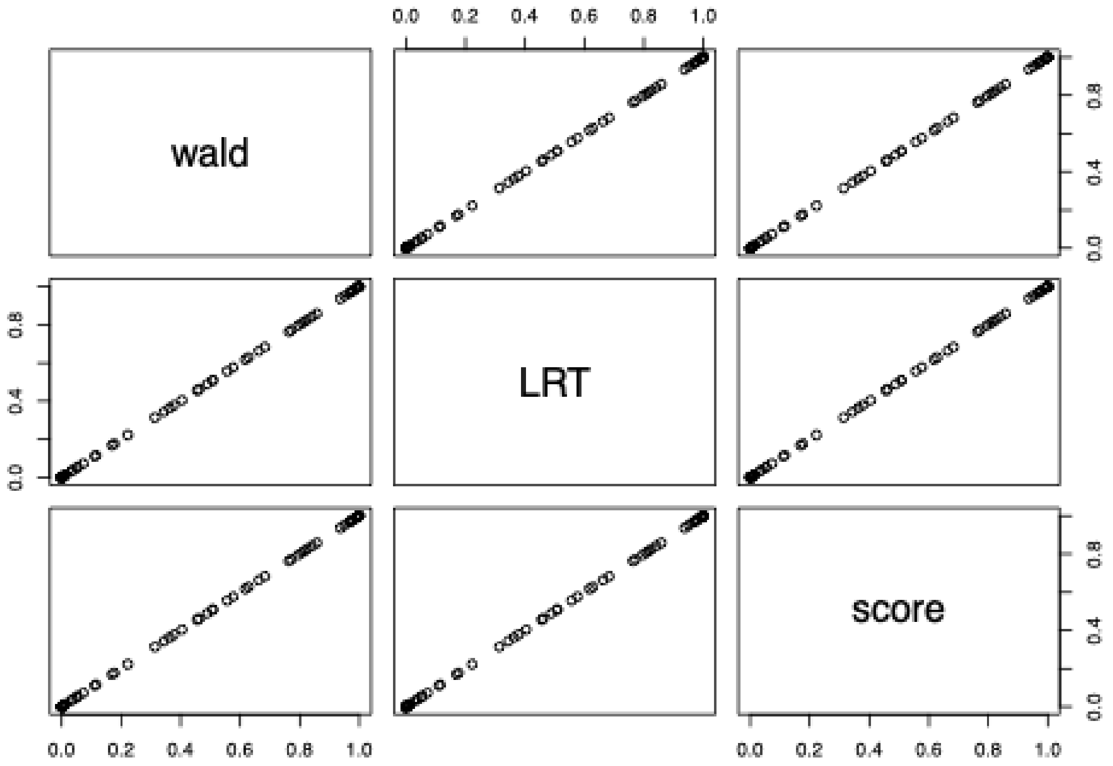


Eigenvalues for each of the 71 spokes using correlation matrix

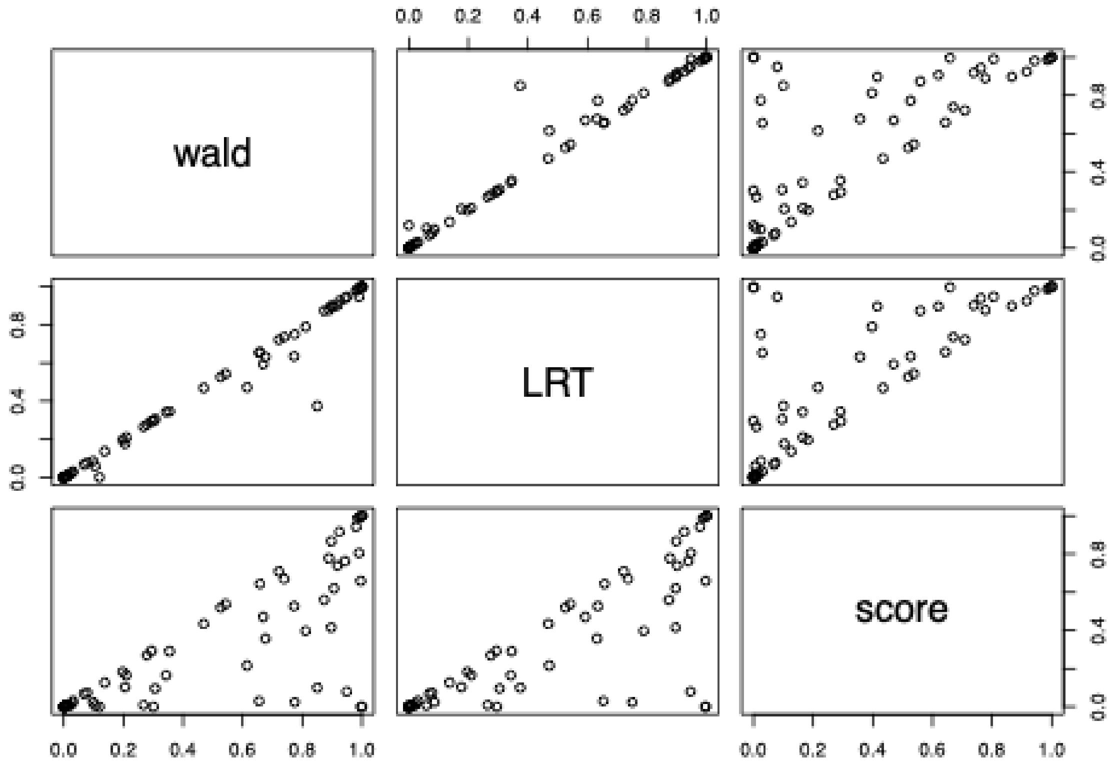


Wald vs LRT vs Score tests

constrained model



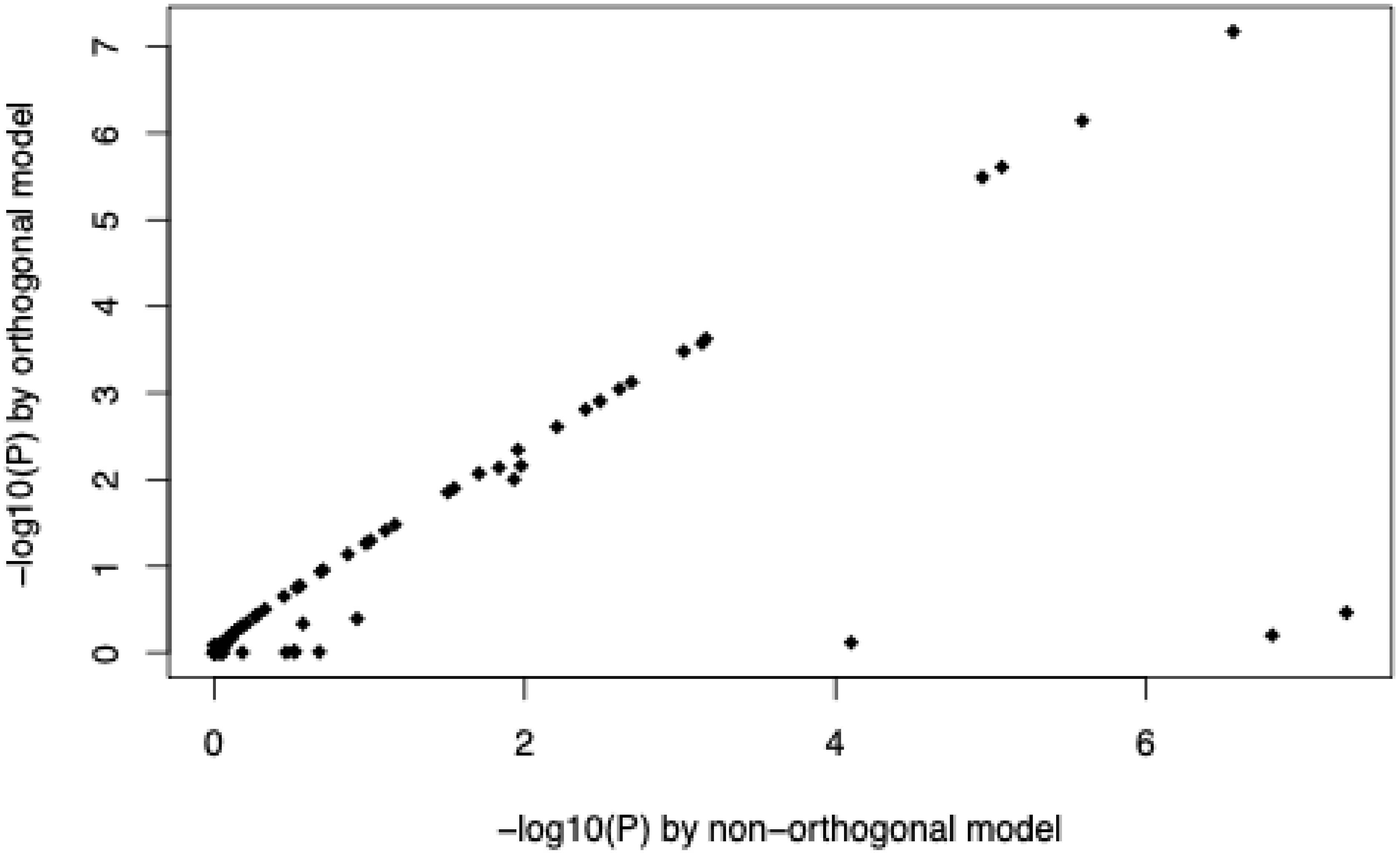
unconstrained model



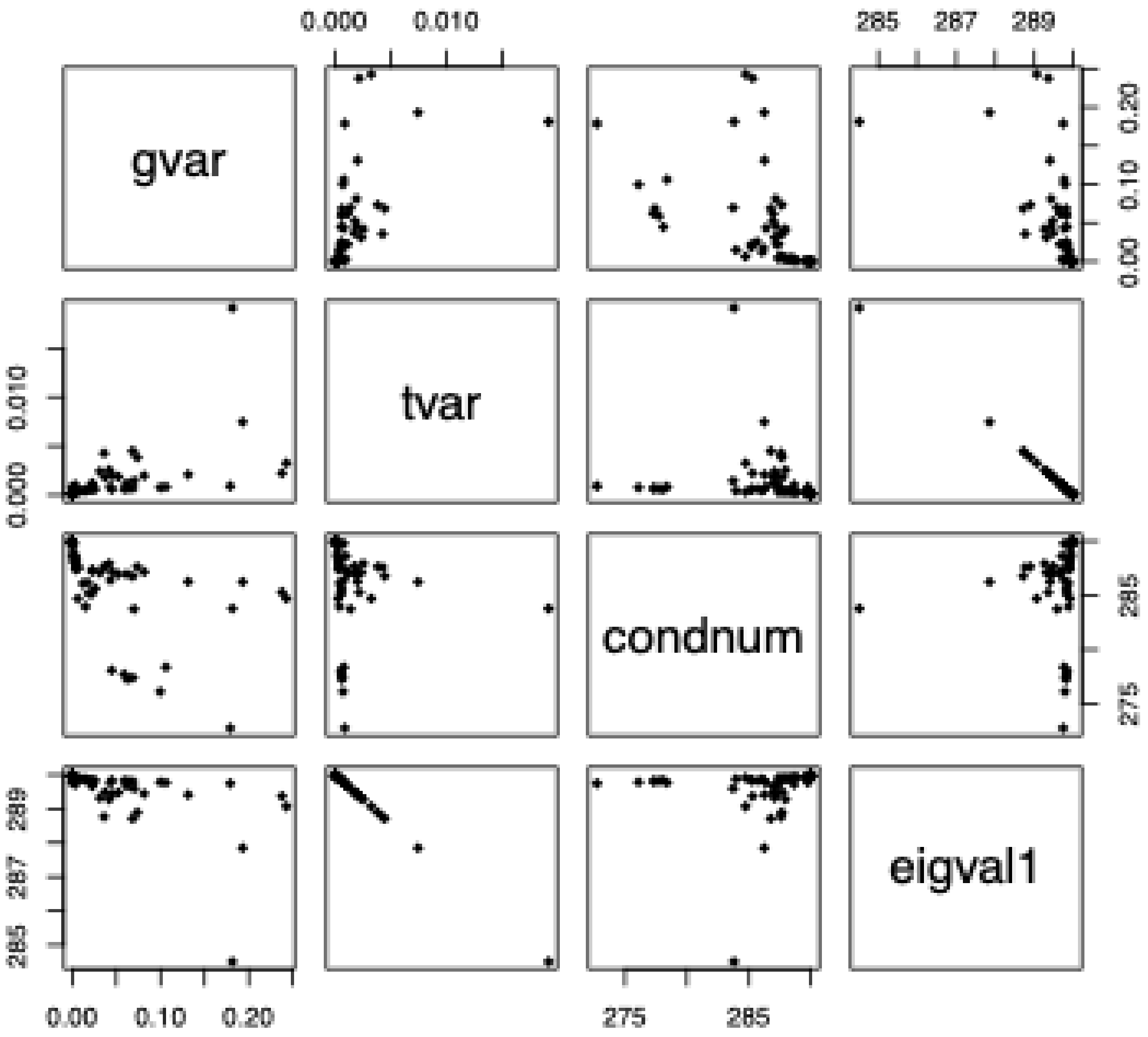
➔ LRT ??

(Wald seems to be conservative in non-ortho model)

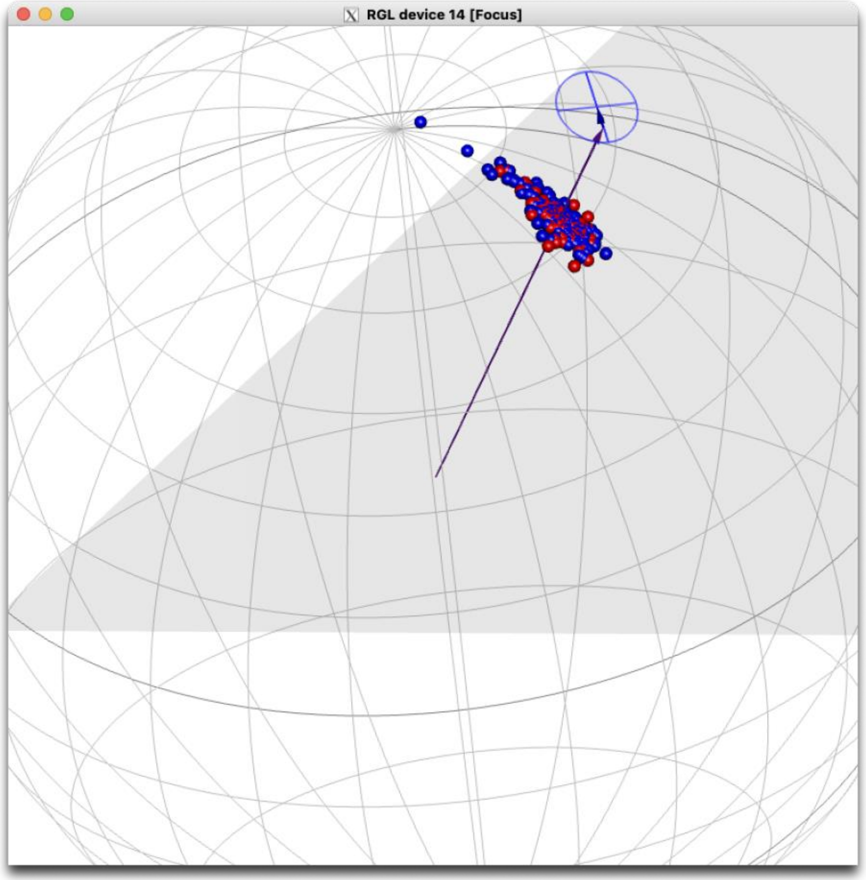
- log10 (p-values) calculated using non-orthogonal and orthogonal models (LRT)

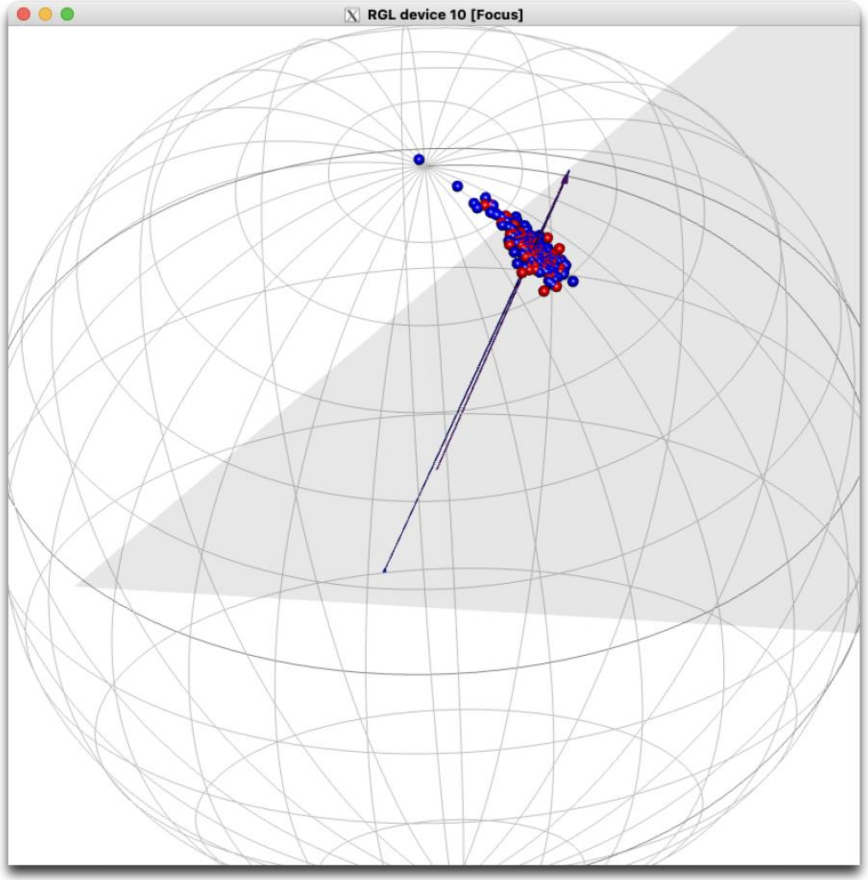


Comparison between covariance matrix criteria



Dispersion only

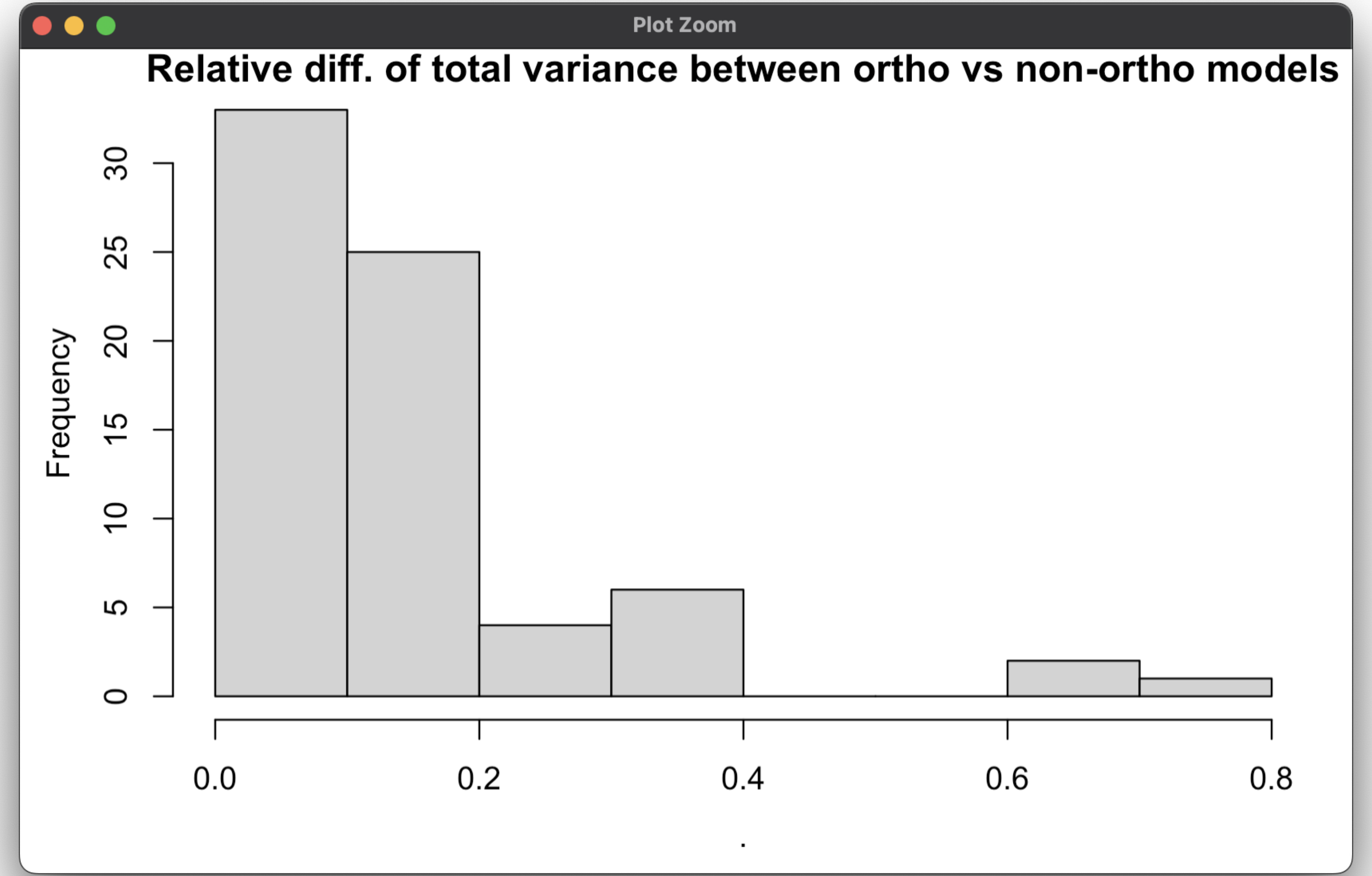




Spoke=38: Dispersion diff. but not Location diff.

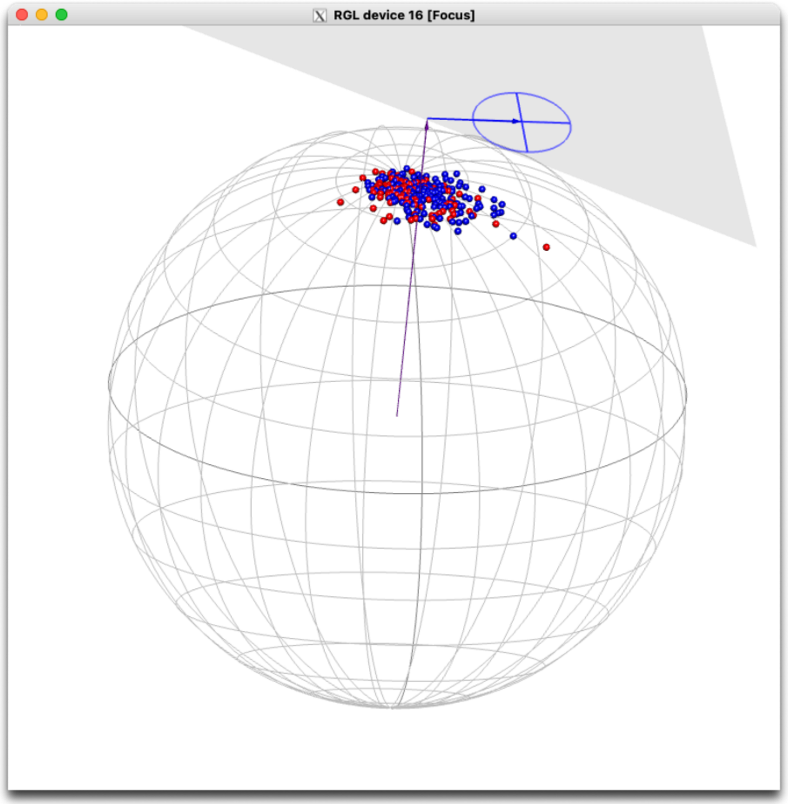
```
> pvalue.array[38,,"LRT"]
   ortho     nonortho
0.404392   0.000382
```

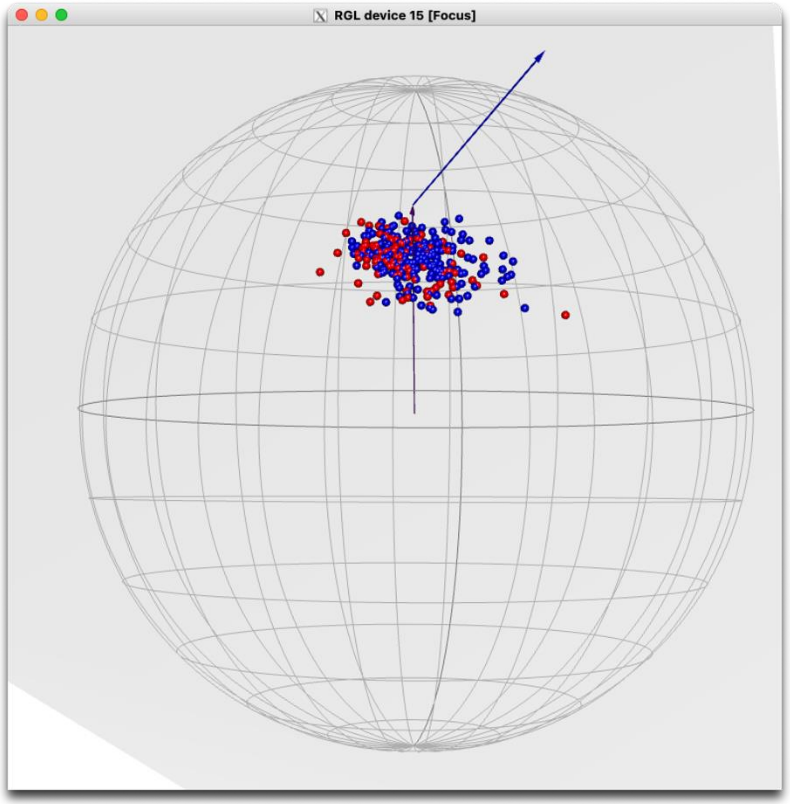
```
> crit.array["tvar",,38]
 Total     group1    group2
0.00184  0.00126  0.00218
```



Plot Zoom
Relative diff. of total variance between ortho vs non-ortho models
Frequency
0
5
10
15
20
25
30
0.0
0.2
0.4
0.6
0.8

Dispersion and Location



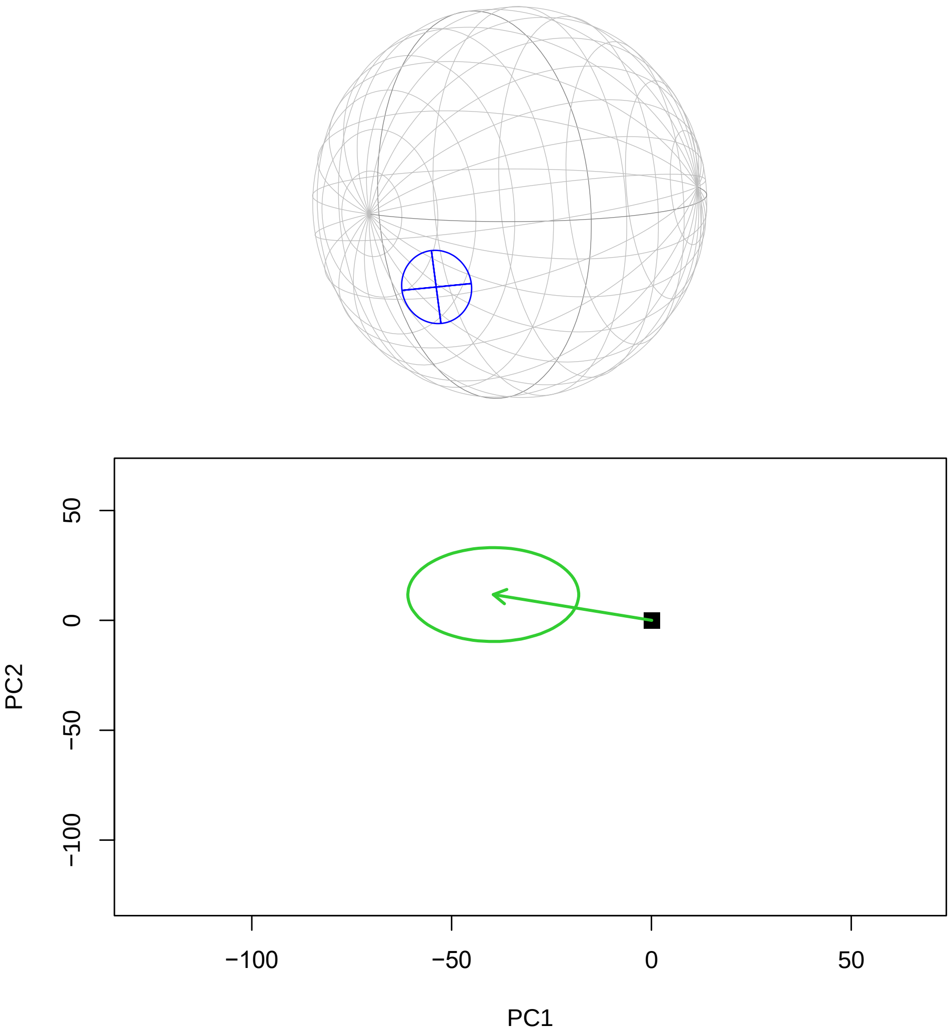


Spoke=9; Location \& Dispersion difference

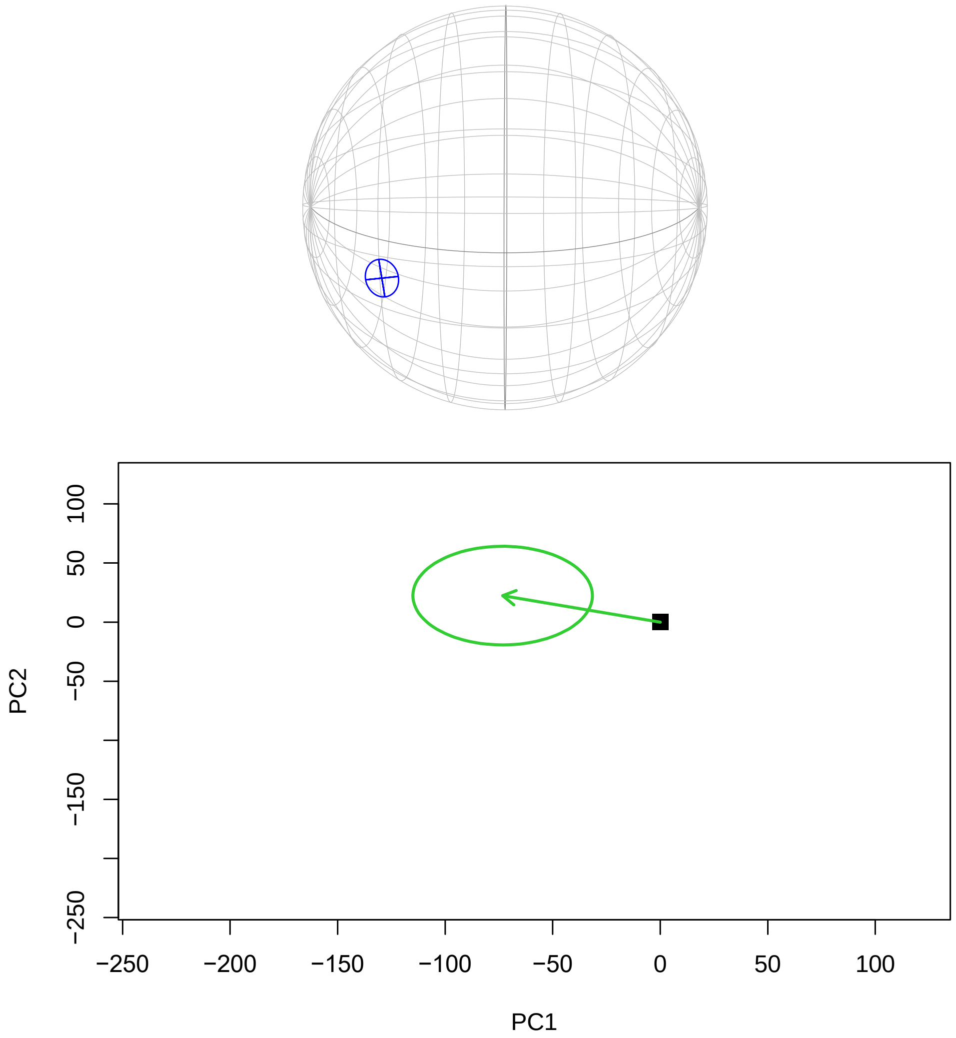
```
> pvalue.array[idx.MeanDiff.VarDiff, , "LRT"]
        ortho        nonortho
spk9    7.186e-07    2.574e-06
spk12   2.463e-06    8.491e-06
spk14   3.222e-06    7.429e-06
spk26   6.668e-08    2.512e-07
```

The two significant spokes were identified by both methods based on the adjusted p-values.

9th spoke

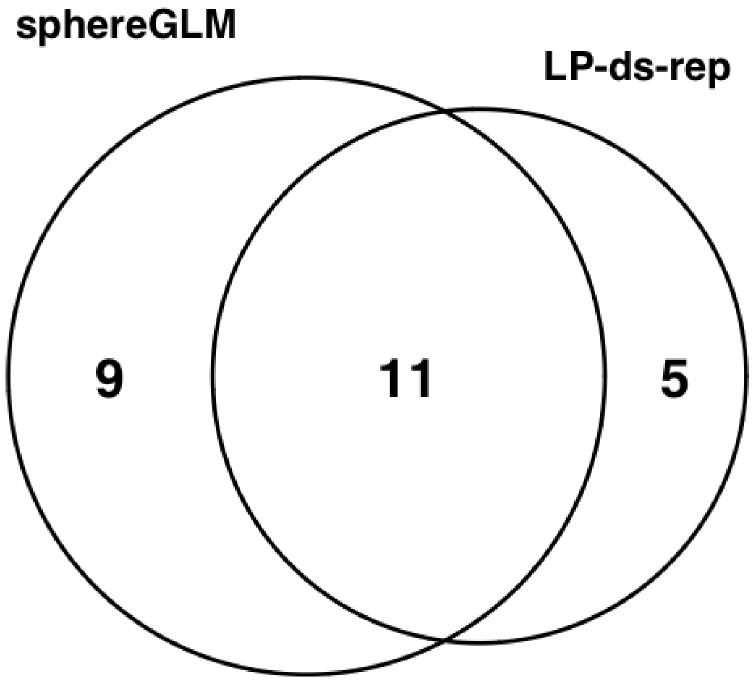


12th spoke

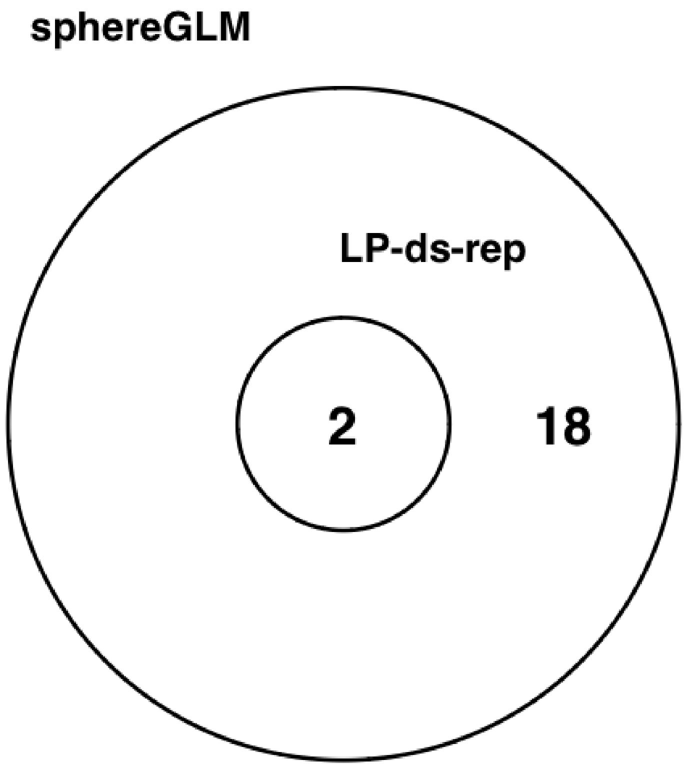


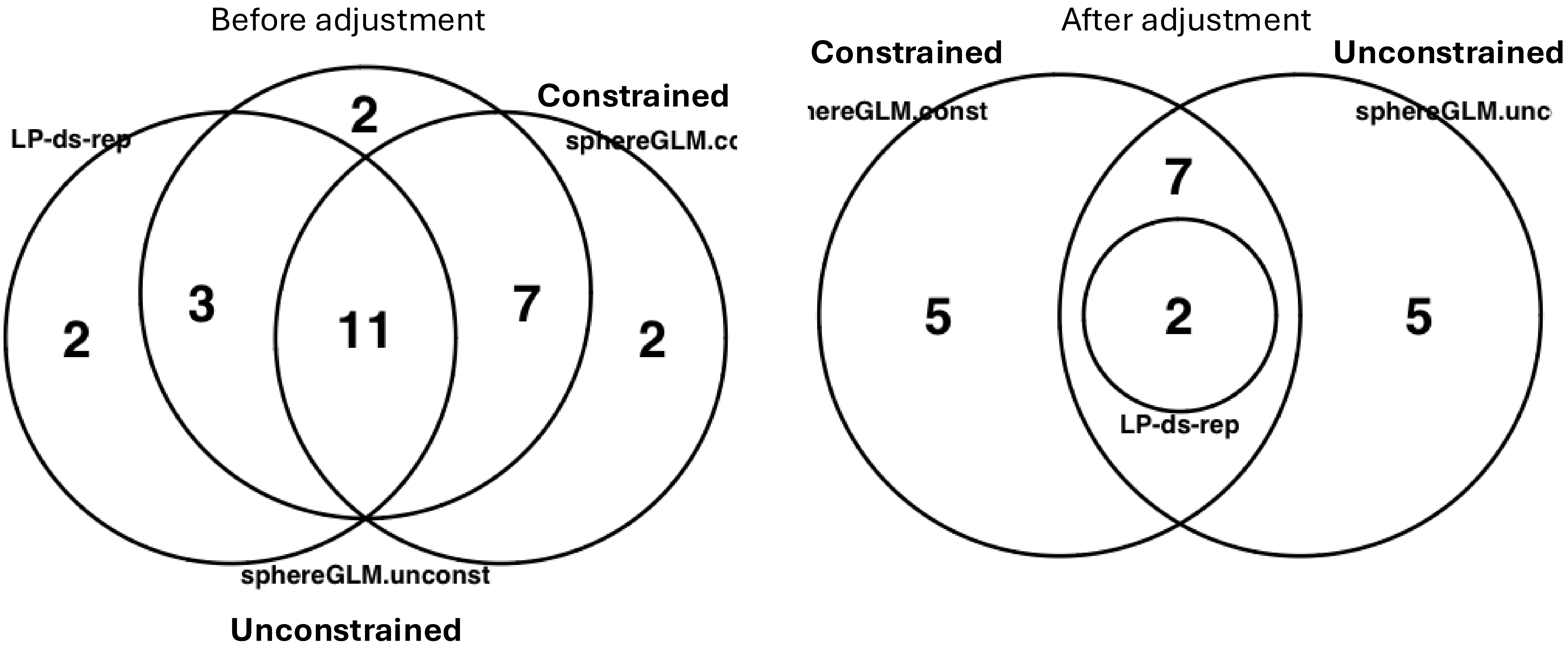
vs LP-ds-rep

Before adjustment



After adjustment




Before adjustment
Constrained
LP-ds-rep
sphereGLM.co
2
3
11
7
2
2
sphereGLM.unconst
Unconstrained
After adjustment
Constrained
Unconstrained
hereGLM.const
sphereGLM.unc
7
5
2
5
LP-ds-rep

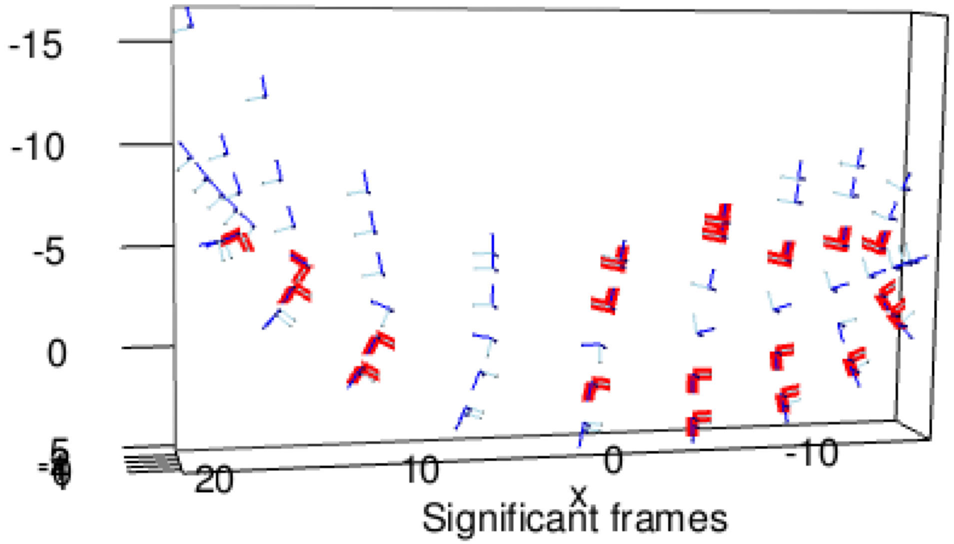
vs LP-ds-rep

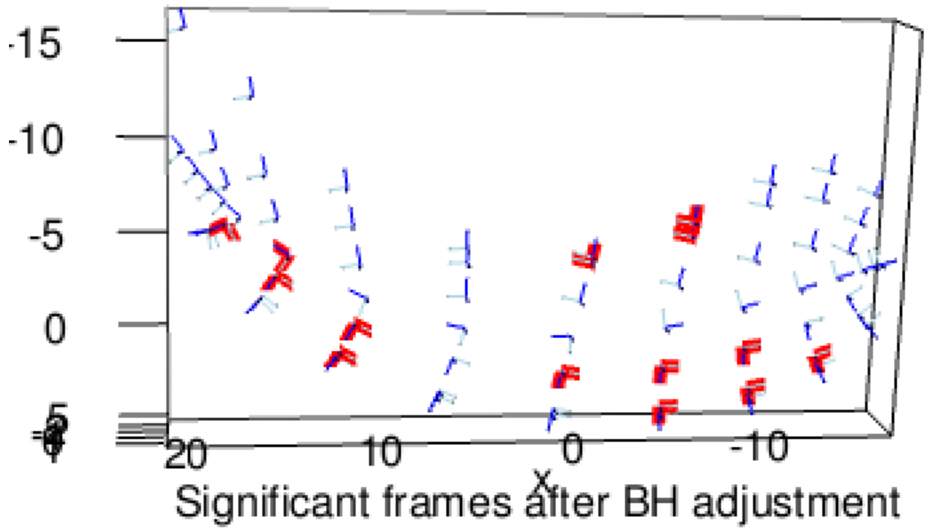
Frames' directions

Before adjustment

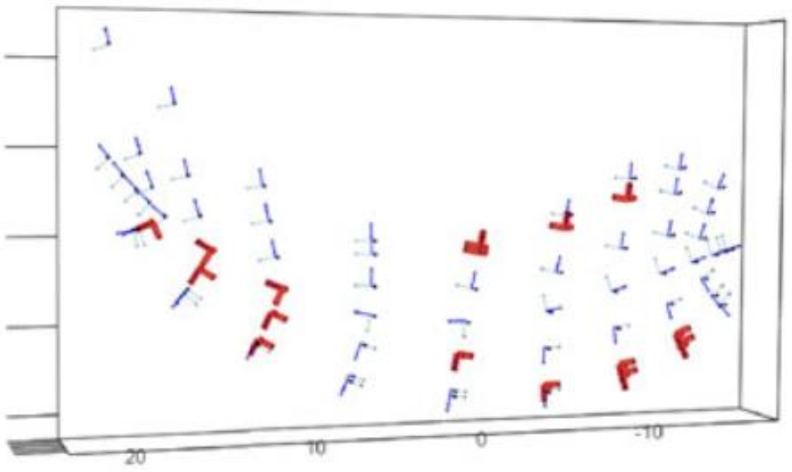
After adjustment

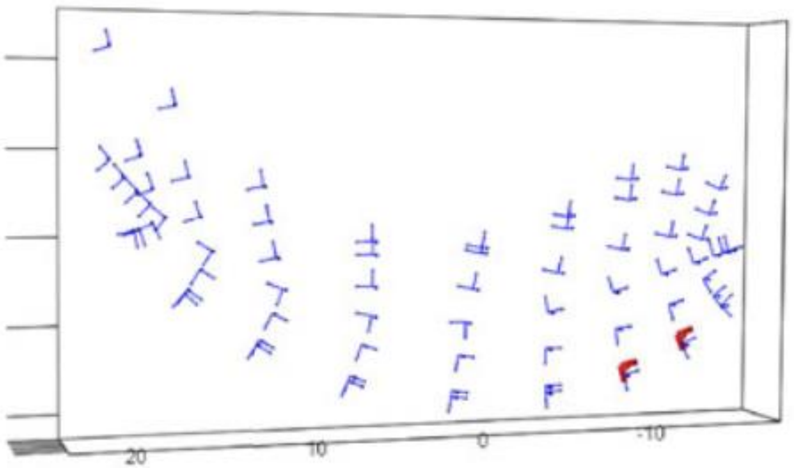
Constrained sphereGLM





LP-ds-rep





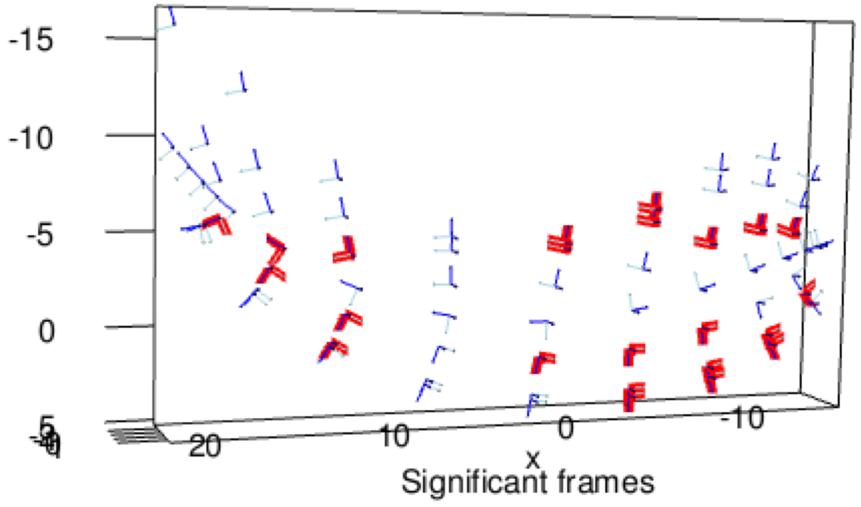
vs LP-ds-rep

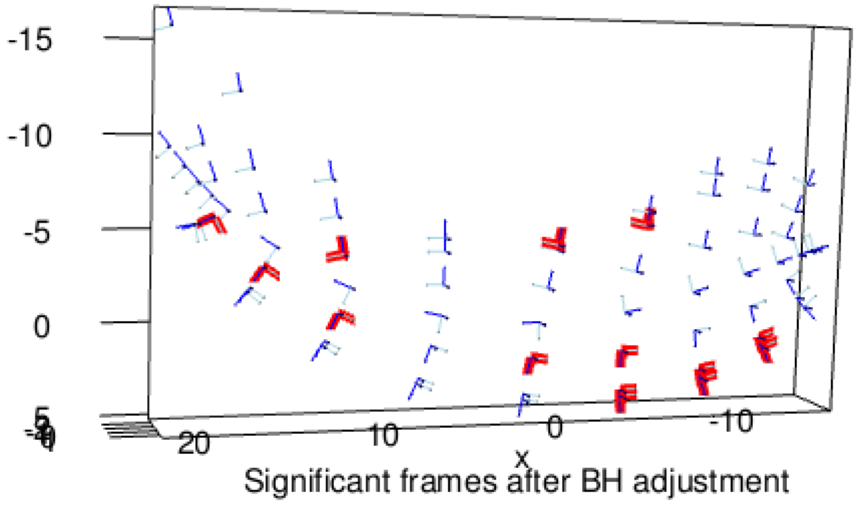
Frames' directions

Before adjustment

After adjustment

Unconstrained sphereGLM





LP-ds-rep