Measures of FMRI Neurologic Synchrony

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Correlation matrix hypotheses, functional connectivity

In neuroscience, it is well known that regions of the brain exhibit functional synchrony. Functional synchrony is characterized by regions of the brain having correlated neural activity. A well established method to describe this synchrony in fMRI is the average cross correlation termed the COSLOF index. The COSLOF has proved useful as a noninvasive quantitative marker of hippocampal synchrony for the preclinical stage of Alzheimer's disease. This paper presents the COMDET, an alternative index of functional synchrony, and compares it to the COSLOF with their statistical underpinnings. The COSLOF and COMDET result from generalized likelihood ratio tests of independence versus intraclass or general correlation structure. Logarithmic functions of these two statistics are presented with their asymptotic chi squared distributions. These two statistics are empirically compared under five correlation structures. It is found that the COMDET performs better than the COSLOF except under the case of a small sample and small correlation. Critical values are presented which are determined via Monte Carlo simulation.

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Outline

+ **Introduction**
+ **Correlation**
+ **Multivariate Model**
+ **COSLOF/COMDET**
+ **Real AD Data**
+ **Comments**

Introduction

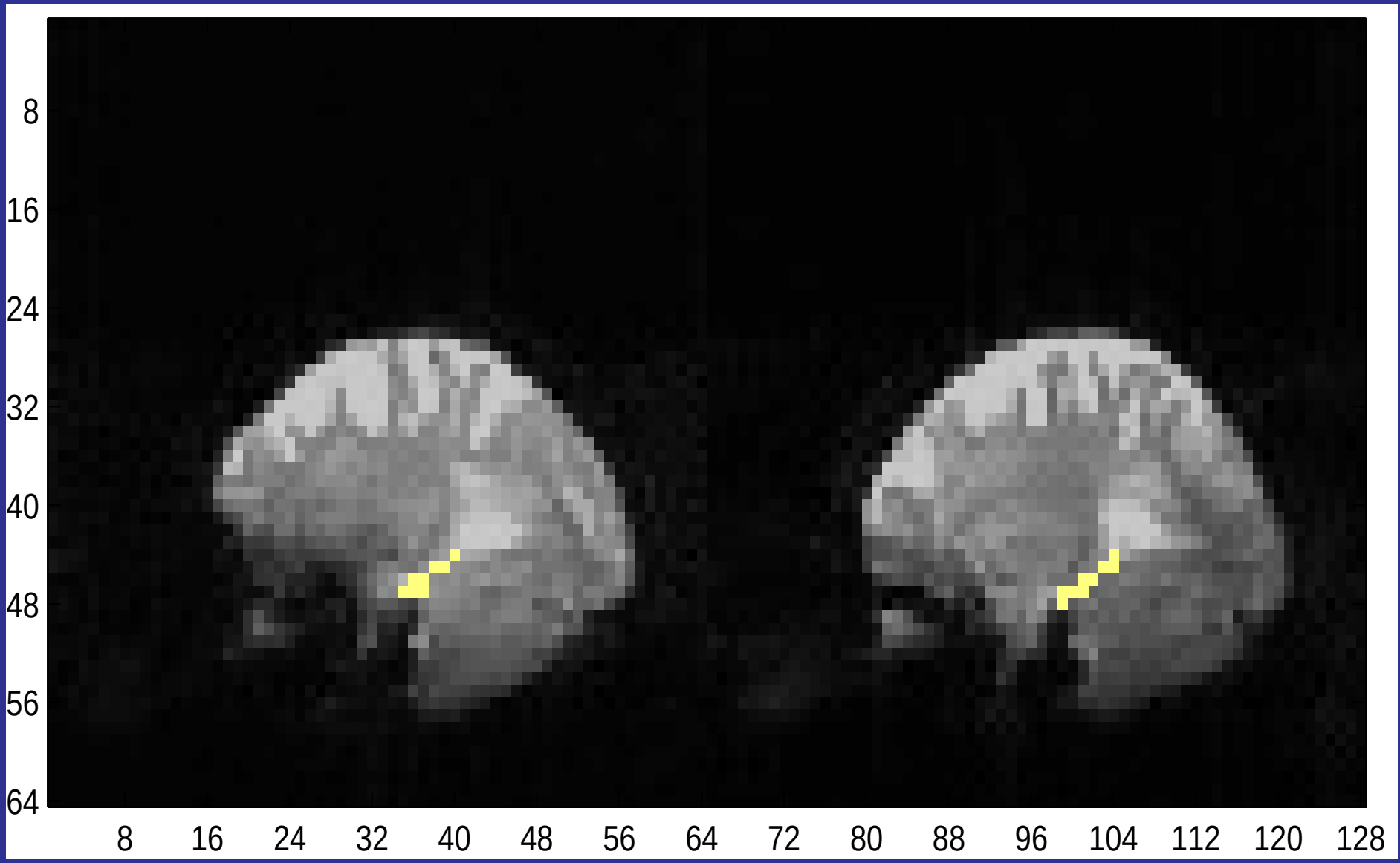
Functional synchrony in fMRI is well known
(Biswal et al. 95, Hyde & Biswal 99).

It has been characterized with resting state cross-correlations.

The COSLOF index (average cross correlation) applied to the hippocampus has been used as a preclinical marker for AD.

Hippocampus is responsible for the storage of declarative (factual) memory and it has been shown that functional synchrony is reduced in Alzheimers disease patients compared to normals (Li et al. 02).

Hippocampi: 8L,9R



Correlation

If $\hat{\Sigma}$ is our estimate of the p-dimensional matrix, then

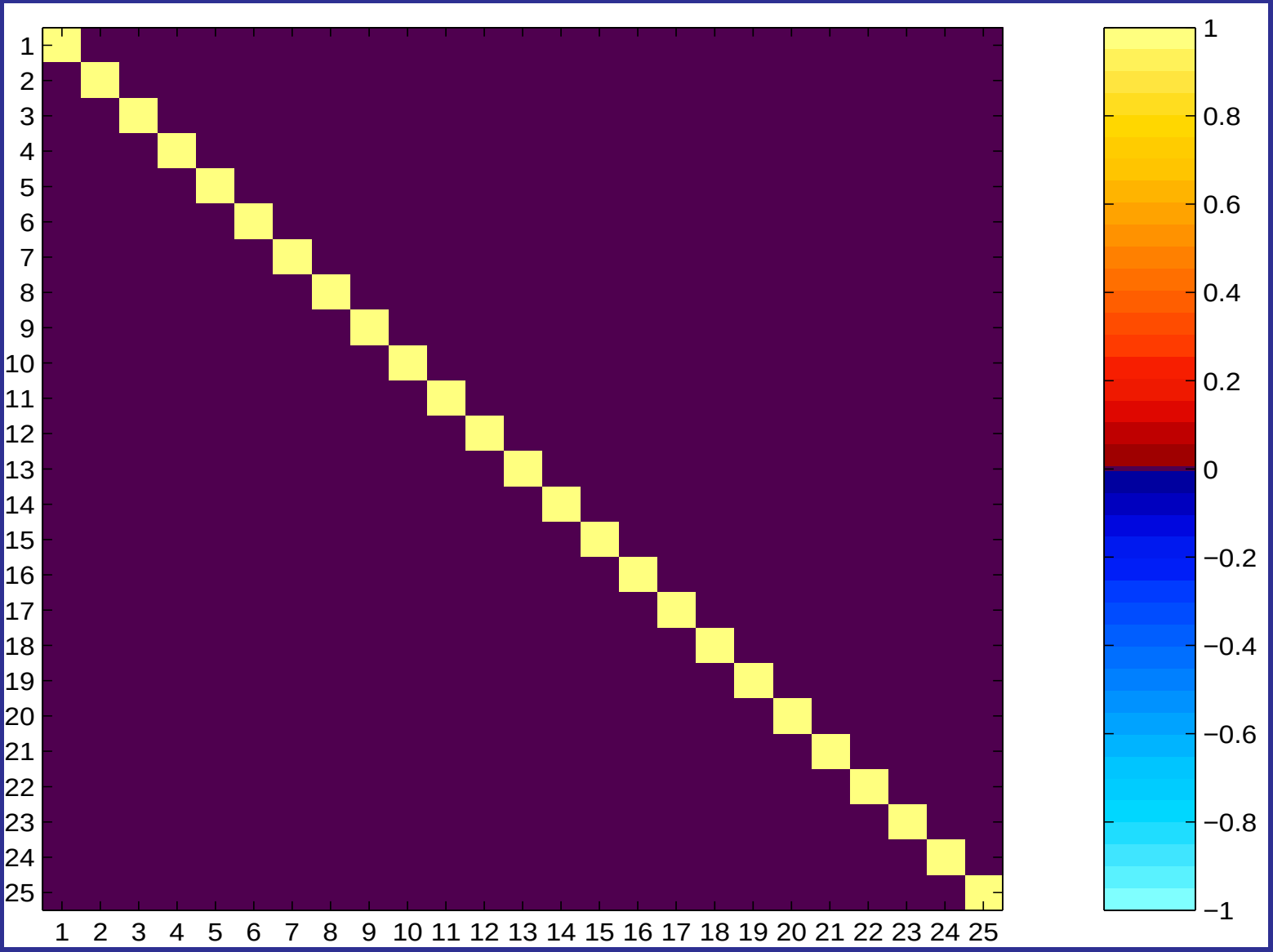
$$\hat{R} = \begin{bmatrix} \hat{\sigma}_1^{-1} & 0 & \dots & 0 \\ 0 & \hat{\sigma}_2^{-1} & & \vdots \\ \vdots & & \ddots & 0 \\ 0 & \dots & 0 & \hat{\sigma}_p^{-1} \end{bmatrix} \begin{bmatrix} \hat{\sigma}_1^2 & \hat{\sigma}_{12} & \dots & \hat{\sigma}_{1p} \\ \hat{\sigma}_{21} & \hat{\sigma}_2^2 & & \vdots \\ \vdots & & \ddots & \hat{\sigma}_{p-1,p-1} \\ \hat{\sigma}_{p1} & \dots & \dots & \hat{\sigma}_p^2 \end{bmatrix} \begin{bmatrix} \hat{\sigma}_1^{-1} & 0 & \dots & 0 \\ 0 & \hat{\sigma}_2^{-1} & & \vdots \\ \vdots & & \ddots & 0 \\ 0 & \dots & 0 & \hat{\sigma}_p^{-1} \end{bmatrix}$$

$$= \hat{D}^{-1/2}\, \hat{\Sigma}\, \hat{D}^{-1/2}$$

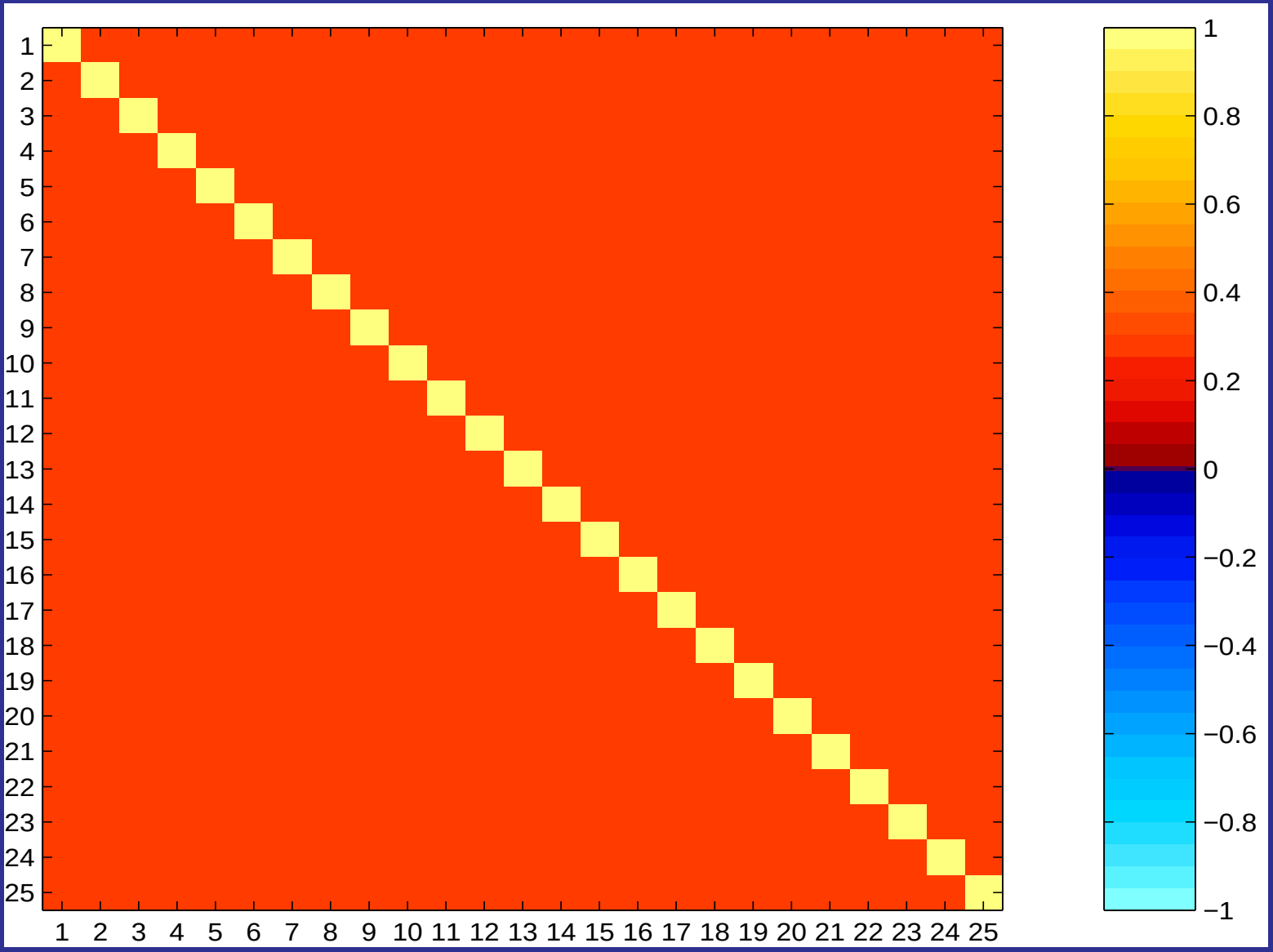
$$\hat{\Sigma} = \hat{D}^{1/2}\, \hat{R}\, \hat{D}^{1/2}$$

An index or statistic of voxel relatedness should be a function of the correlation matrix!

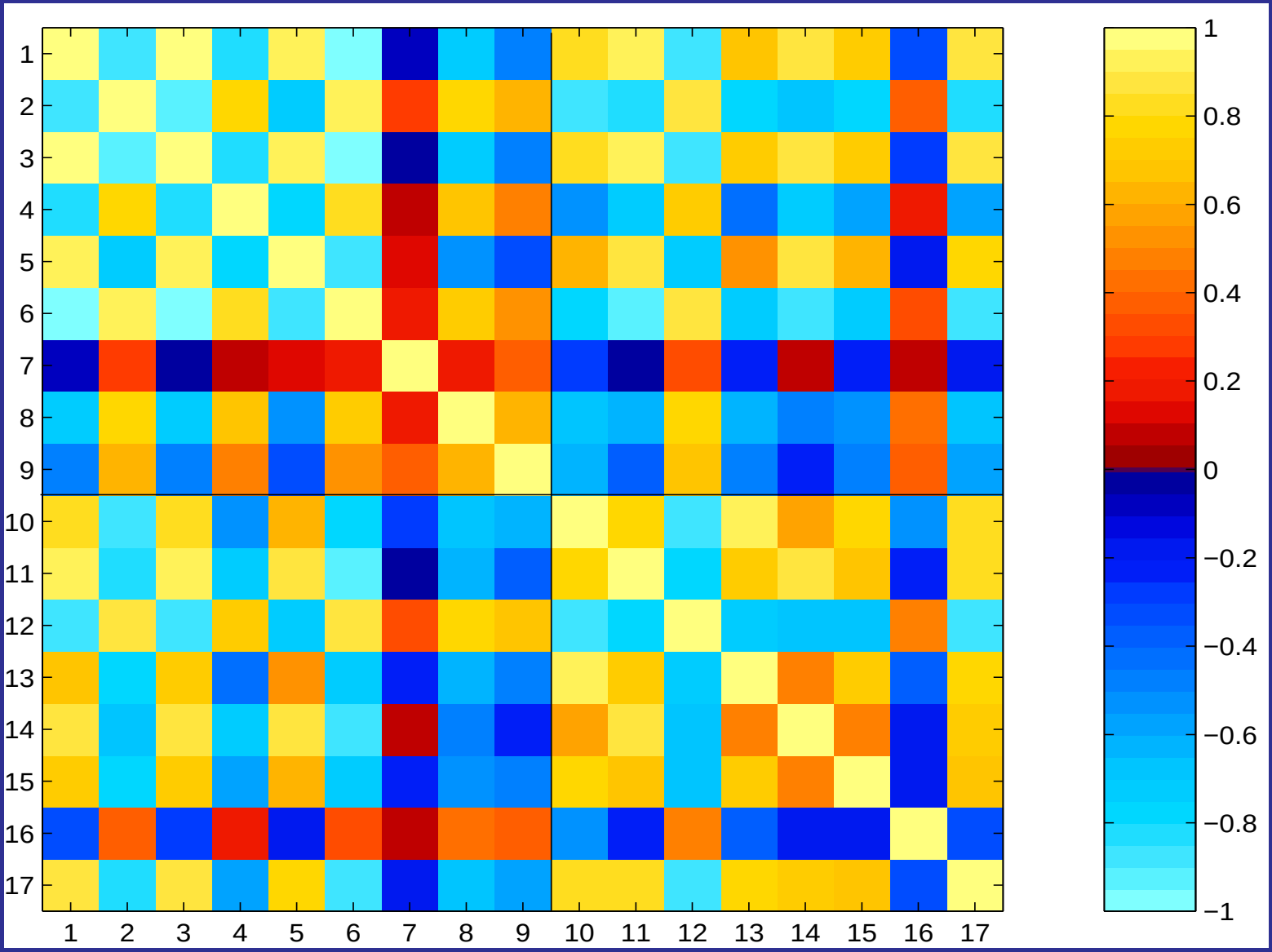
Correlation Matrix: Independent



Correlation Matrix: Intraclass .3



Correlation Matrix: General



Multivariate Model

Use the standard multivariate linear regression model (Rowe 02) for p voxels measured at n time points

$$\underset{n \times p}{Y} = \underset{n \times (q+1)}{X} \underset{(q+1) \times p}{B} + \underset{n \times p}{E}$$

Y is the matrix of observed time courses,
X is the design matrix,
B is the matrix of regression coefficients, and
E is the matrix of errors.
Assuming $vec(E') \sim N(0, I_n \otimes \Sigma)$, the likelihood is

$$p(Y|B, \Sigma, X) = (2\pi)^{-\frac{np}{2}} |\Sigma|^{-\frac{n}{2}} e^{-\frac{1}{2} tr \Sigma^{-1} (Y - XB)'(Y - XB)}.$$

Intraclass Correlation Test

$$\begin{array}{rrcl} H_0: & B & \in \mathbb{R}^{(q+1)\times p} & vs \\ & \mathrm{diag}(D) & = \mathbb{R}^{p+} & \\ & R & = I_p & \end{array} \quad \begin{array}{rrl} H_1: & B & \in \mathbb{R}^{(q+1)\times p} \\ & \mathrm{diag}(D) & = \mathbb{R}^{p+} \\ & R & = (1-\rho)I_p + \rho e_p e_p' \end{array}$$

The GLR statistic is

$$\lambda = \frac{p(Y|\tilde{B},\tilde{D},\tilde{\rho},X)}{p(Y|\hat{B},\hat{D},\hat{\rho},X)}$$

$$\hat{\rho} \doteq \frac{\lambda^{2/n}-1}{\lambda^{2/n}+p-1}$$

The COSLOF is $\hat{\rho} = (e_p \hat{R} e_p' - p)/[p(p-1)]$

General Correlation Test

$$\begin{array}{rrcl} H_0: & B & \in \mathbb{R}^{(q+1)\times p} & vs \\ & \mathrm{diag}(D) & = \mathbb{R}^{p+} & \\ & R & = I_p & \end{array} \quad \begin{array}{rrcl} H_1: & B & \in \mathbb{R}^{(q+1)\times p} & \\ & \mathrm{diag}(D) & = \mathbb{R}^{p+} & \\ & R & \neq I_p & \end{array}$$

The GLR statistic is

$$\lambda = \frac{p(Y|\tilde{B},\tilde{\Sigma},X)}{p(Y|\hat{B},\hat{\Sigma},X)}$$

$$\lambda^{\frac{2}{n}} = |\hat{R}|$$

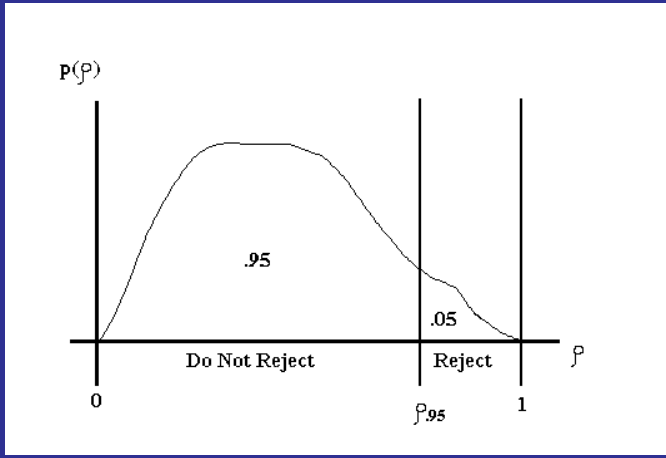
The COMDET is $\hat{\varrho} = |\hat{R}|$.

Test Statistics

COSLOF: $\hat{\rho} = (e_p \hat{R} e_p' - p)/[p(p-1)]$

COMDET: $\hat{\varrho} = |\hat{R}|$

How do we determine what a large COSLOF or small COMDET is?



Typically we would know the distribution of the test statistic so that if our value were in the upper or lower tail with probability $\alpha = .05$ we would reject the null hypothesis.

Significance

So what are we to do? Compute
$u = -2 \ln \lambda_{\hat{\rho}} \dot{\sim} \chi^2(1)$
$v = -2[\nu - (2p+5)/6]/n \ln \lambda_{\hat{\varrho}} \dot{\sim} \chi^2(p(p-1)/2)$
$\nu = n - q - 1$, but when do asymptotic distributions hold?

Deterministic critical values v, limited (ν, p), Mathai & Katiyar, 1979.

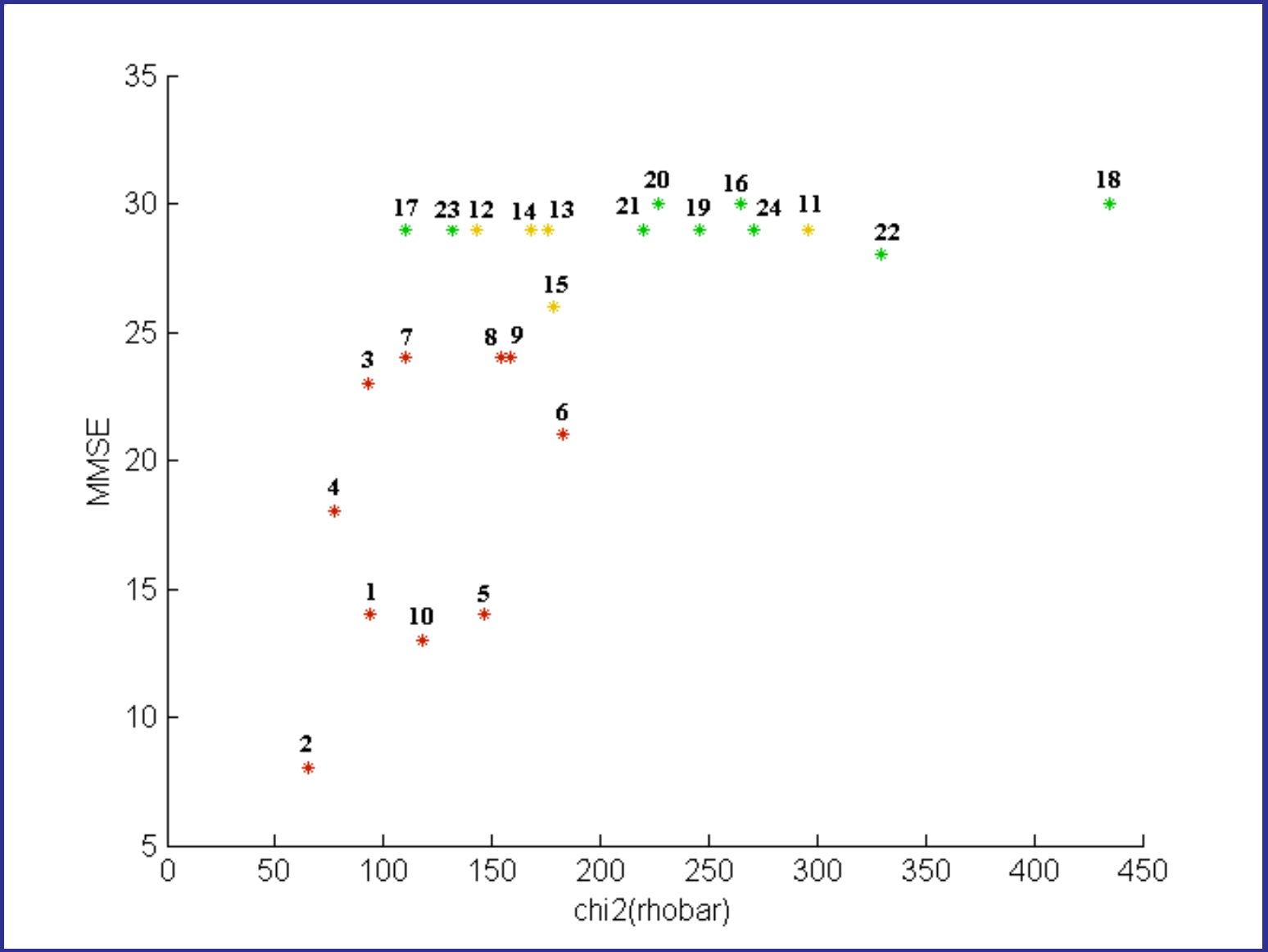
Monte Carlo critical values u and v, expanded (ν, p), Rowe, 2003.

Can also assess asymptotic results (ν, p), Rowe, 2003.

Real AD Data

Imaging Parameters:
1.5T GE Signa
$TR = 2000ms,\ \ TE = 40ms$
GRE 15 Sagittal Slices
$64 \times 64,\ \ FOV = 24cm$
$3.75 \times 3.75 \times 7mm$
$n = 180$

Best slice through each Hippocampus selected and voxels extracted.
Time series low pass filtered and linear model fit.
Correlation matrix computed from residuals.


MMSE
chi2(rhobar)
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400
450
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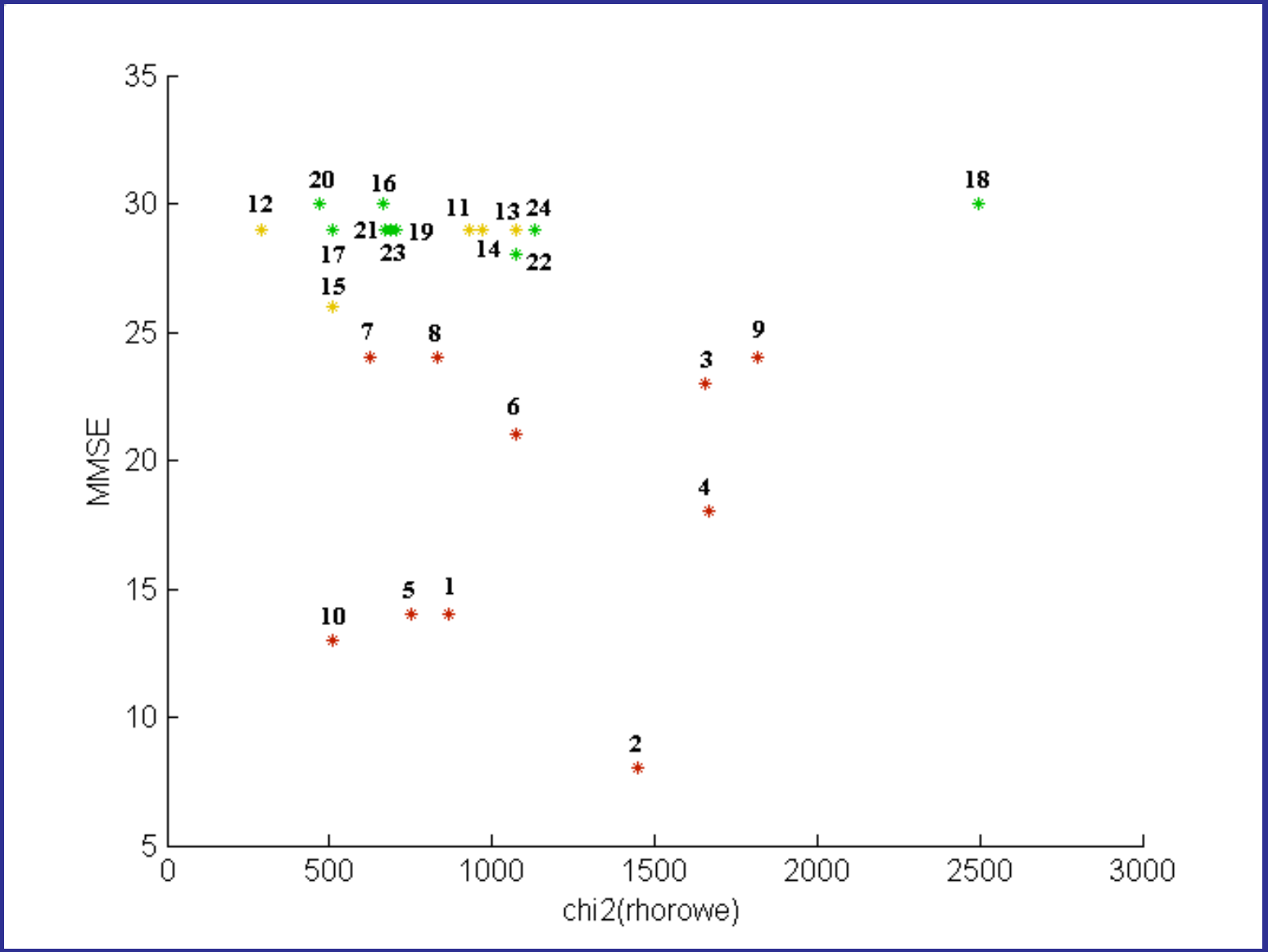
MMSE
chi2(rhorowe)
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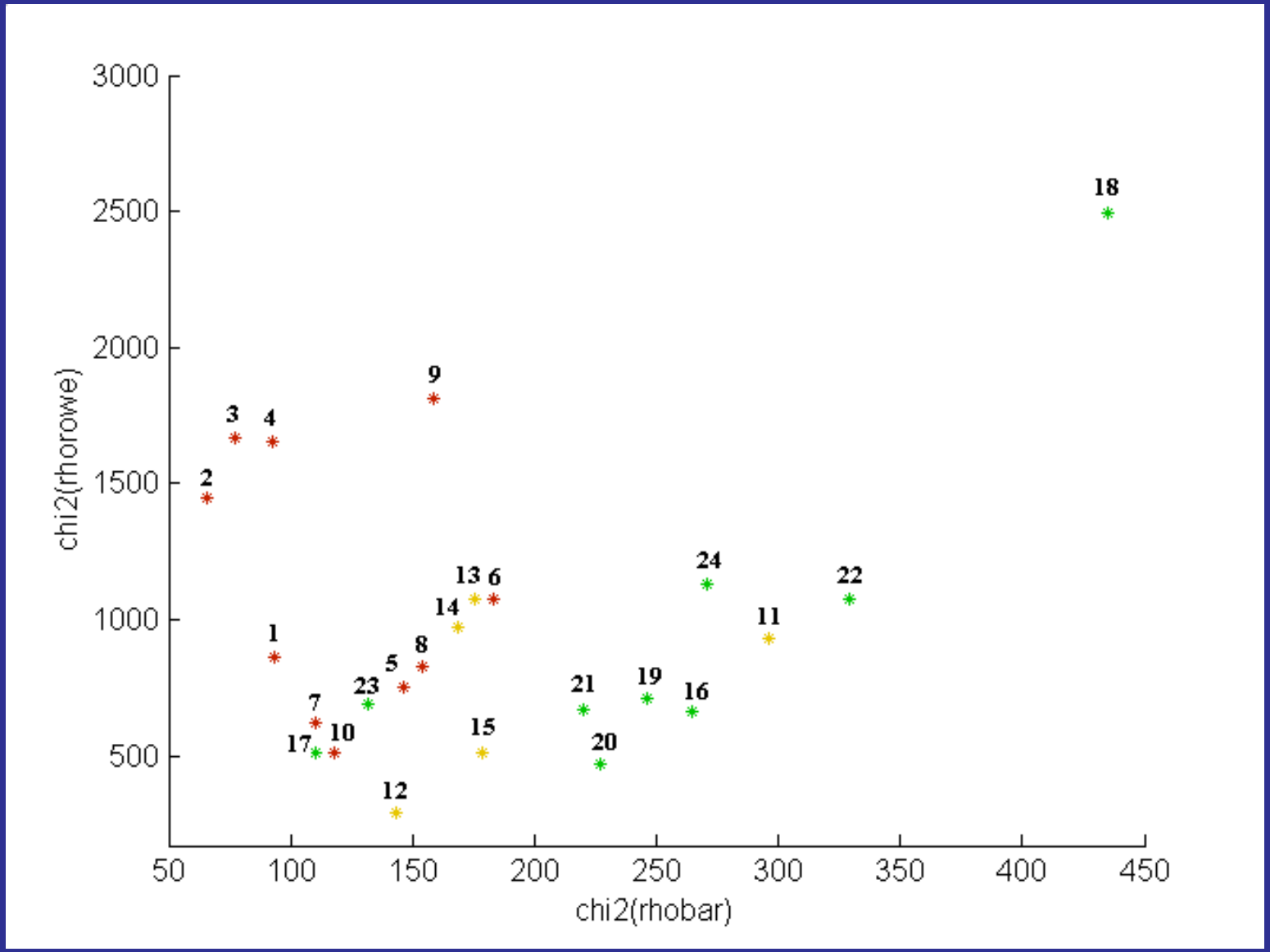
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Conclusion

Presented the current index

Presented a new index

Using both can be useful

Thanks to Dr. S.J. Li of MCW for the data.