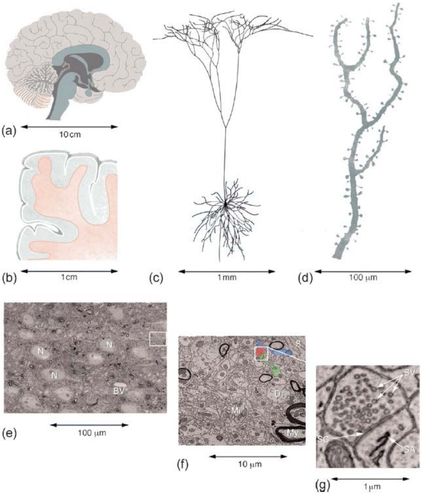
Multivariate Linear Models

Bratislav Mišić

NEUR 603

March 21^{st} 2018

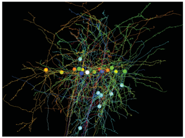
Multi-scale neural circuits



Lichtman & Denk (2011) *Science*

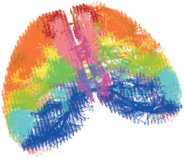
Imaging neural circuits

electron microscopy



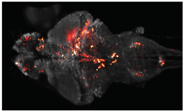
Bock et al. (2011) Nature

tract tracing



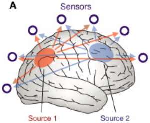
Oh et al. (2014) Nature

calcium imaging



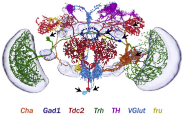
Ahrens et al. (2013) Nat Meth

M/EEG



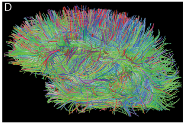
Engel et al. (2013) Neuron

genetic labeling



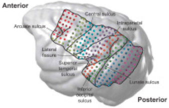
Chiang et al. (2011) Curr Biol

diffusion imaging



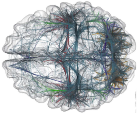
Hagmann et al. (2007) PLoS ONE

electrophysiology



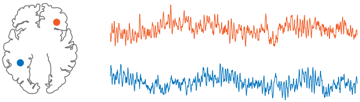
Bastos et al. (2015) Neuron

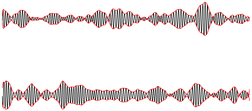
haemodynamics



Boettger et al. (2014)
IEEE Trans Vis Comput

Estimating functional connectivity

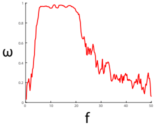




amplitude coupling

Brookes et al (2012) NeuroImage

Hipp et al (2012) Nat Neurosci

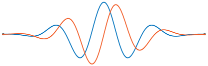


spectral coupling

Nolte et al (2004) J Clin Neurophysiol

Baccala & Sameshima (2001) Biol Cybern

Kaminski & Blinowska (1991) Biol Cybern



phase coupling

Lachaux et al (1999) Hum Brain Mapp

Stam et al (2007) Hum Brain Mapp

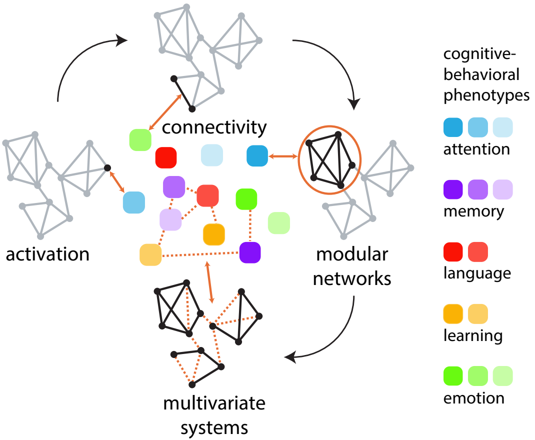
Vinck et al (2011) NeuroImage

Niso et al. (2013) *Neuroinformatics*

Bastos & Schoffelen (2016) *Front Syst Neurosci*

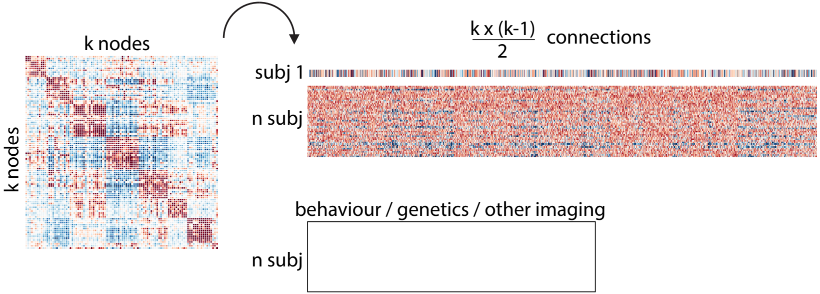
Colcough et al. (2016) *NeuroImage*

Towards multivariate analysis



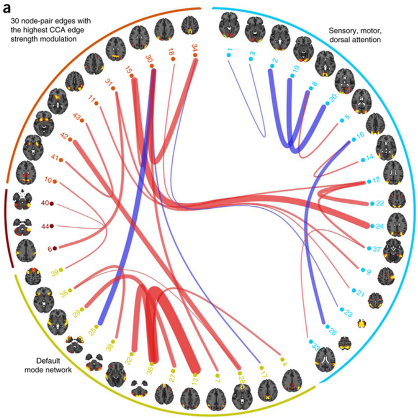
Mišić & Sporns (2016) *Curr Opin Neurobiol*

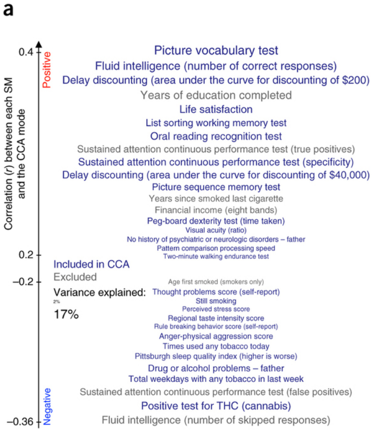
Why multivariate statistics?



1. how to operationalize network property?
2. how to deal with with more variables than observations?
3. how to relate multiple data sets to one another?

Example: relating connectivity and behaviour



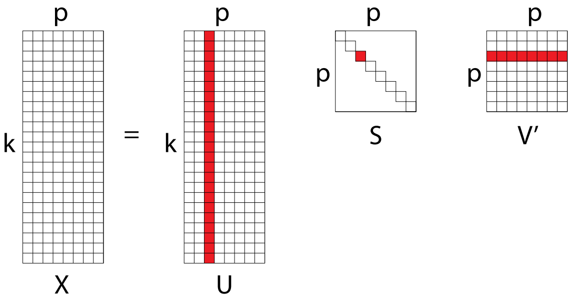


Smith et al. (2015) *Nat Neurosci*

Singular value decomposition

Spectral decomposition:
$\mathrm{EIG}(\mathbf{X}'\mathbf{X}) = \mathbf{U\Lambda U}'$
$\mathrm{EIG}(\mathbf{XX}') = \mathbf{V\Lambda V}'$

Singular value decomposition:
$\mathrm{SVD}(\mathbf{X}) = \mathbf{USV}'$



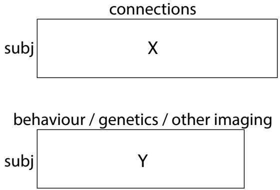
Eckart & Young (1936) *Psychometrika*

A family of techniques

PCA: SVD($\mathbf{X}$)

PLS: SVD($\mathbf{X}'\mathbf{Y}$)

CCA: SVD($(\mathbf{X}'\mathbf{X}')^{-1/2}(\mathbf{X}'\mathbf{Y})(\mathbf{Y}'\mathbf{Y})^{-1/2}$)

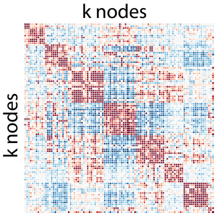


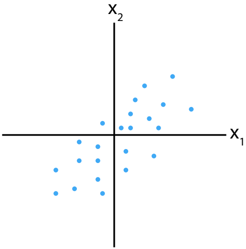
Worsley et al. (1997) *NeuroImage*

De Bie et al. (2005) *Handbook of Geometric Computing - Springer*

McIntosh & Mišić (2013) *Annu Rev Psychol*

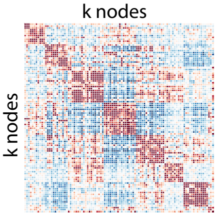
Principal component analysis (PCA)

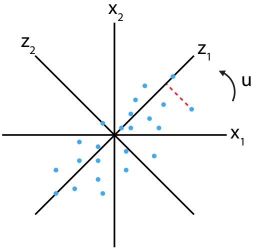




Hotelling (1933) *J Educ Psychol*

Principal component analysis (PCA)





Hotelling (1933) *J Educ Psychol*

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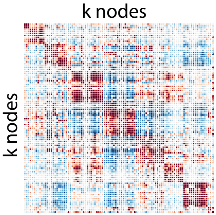

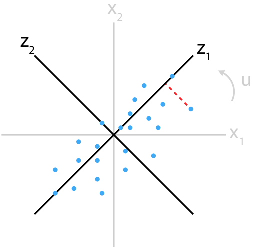

Hotelling (1933) *J Educ Psychol*

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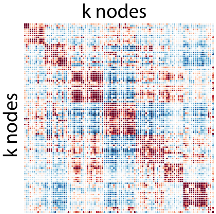

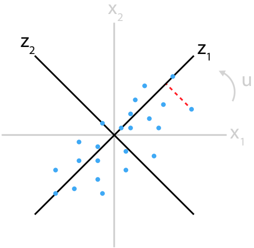

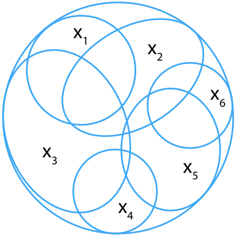

Hotelling (1933) *J Educ Psychol*

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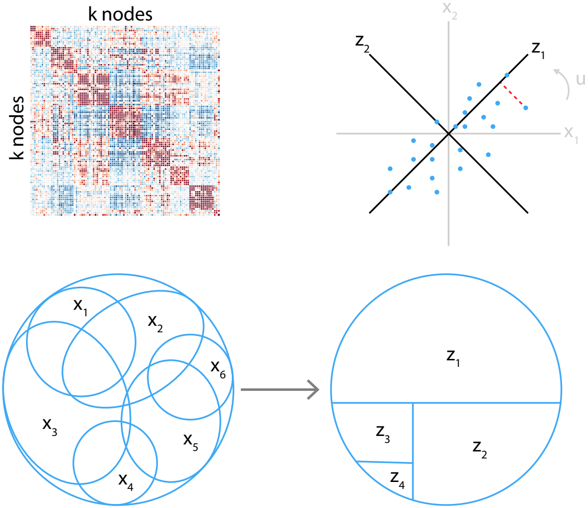
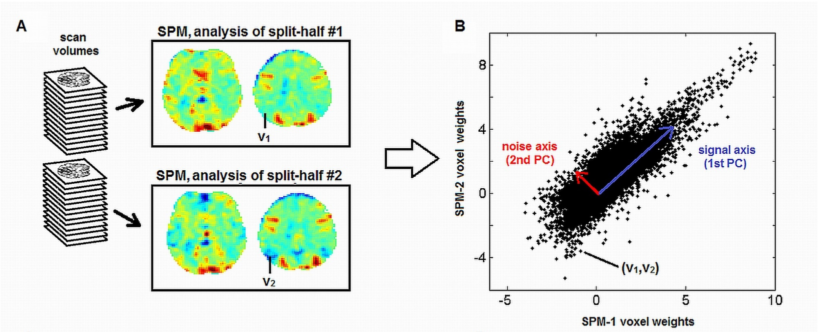


Hotelling (1933) *J Educ Psychol*

Example: PCA of voxel activations



Churchill et al. (2012) *PLoS ONE*

Maximizing variance

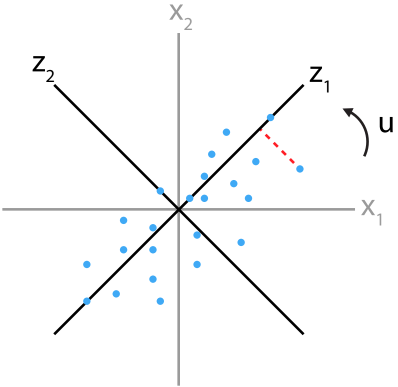
find new variable $\mathbf{z} = \mathbf{X}\mathbf{u}$

choose $\mathbf{u}$ to maximize $var(\mathbf{z})$

under the constraint $\mathbf{u}'\mathbf{u} = 1$

$var(\mathbf{z}) = \frac{1}{n-1}\mathbf{u}'\mathbf{X}'\mathbf{X}\mathbf{u} = \mathbf{u}'\mathbf{R}\mathbf{u}$

since $\mathbf{R} = \frac{1}{n-1}\mathbf{X}'\mathbf{X}$



Maximizing variance

$L = \mathbf{u}'\mathbf{R}\mathbf{u} - \lambda(\mathbf{u}'\mathbf{u} - 1)$

$\frac{\partial L}{\partial \mathbf{u}} = 2\mathbf{R}\mathbf{u} - 2\mathbf{u}\lambda = 0$

$\mathbf{R}\mathbf{u} = \mathbf{u}\lambda$

$(\mathbf{R} - \lambda\mathbf{I})\mathbf{u} = 0$

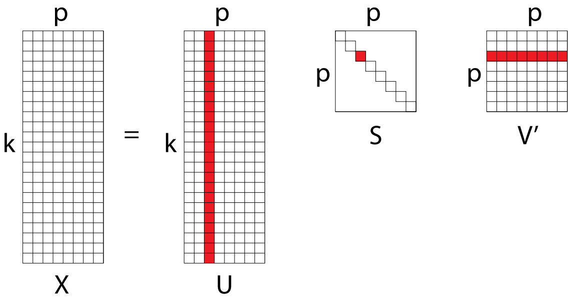
eigenvalue λ (variance) & eigenvector $\mathbf{u}$ (weights)

$var(\mathbf{z}) = \mathbf{u}'\mathbf{R}\mathbf{u} = \mathbf{u}'\mathbf{u}\lambda = \lambda$

Singular value decomposition

Spectral decomposition:
$\mathrm{EIG}(\mathbf{X}'\mathbf{X}) = \mathbf{U}\mathbf{\Lambda}\mathbf{U}'$
$\mathrm{EIG}(\mathbf{X}\mathbf{X}') = \mathbf{V}\mathbf{\Lambda}\mathbf{V}'$

Singular value decomposition:
$\mathrm{SVD}(\mathbf{X}) = \mathbf{U}\mathbf{S}\mathbf{V}'$



Eckart & Young (1936) *Psychometrika*

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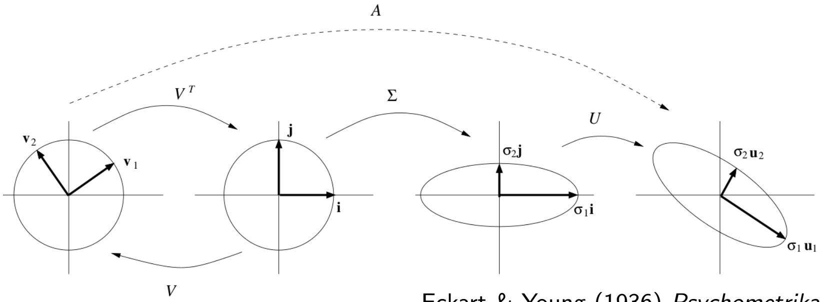


Eckart & Young (1936) *Psychometrika*

EIG vs SVD

SVD: $\mathbf{X} = \mathbf{U}\mathbf{S}\mathbf{V}'$

$$
\begin{aligned}
\text{EIG: } \mathbf{X}'\mathbf{X} &= (\mathbf{V}\mathbf{S}'\mathbf{U}')(\mathbf{U}\mathbf{S}\mathbf{V}') \\
&= \mathbf{V}\mathbf{S}'(\mathbf{U}'\mathbf{U})\mathbf{S}\mathbf{V}' \\
&= \mathbf{V}(\mathbf{S}'\mathbf{S})\mathbf{V}'
\end{aligned}
$$

$$
\begin{aligned}
\text{EIG: } \mathbf{X}\mathbf{X}' &= (\mathbf{U}\mathbf{S}\mathbf{V}')(\mathbf{V}\mathbf{S}'\mathbf{U}') \\
&= \mathbf{U}\mathbf{S}(\mathbf{V}'\mathbf{V})\mathbf{S}'\mathbf{U}' \\
&= \mathbf{U}(\mathbf{S}\mathbf{S}')\mathbf{U}'
\end{aligned}
$$

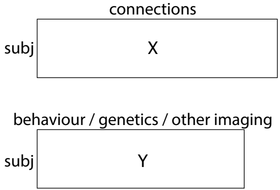
1. eigenvector of $(\mathbf{X}\mathbf{X}')$ = left singular vector $(\mathbf{U})$
2. eigenvector of $(\mathbf{X}'\mathbf{X})$ = right singular vector $(\mathbf{V})$
3. eigenvalue = squared singular value

A family of techniques

PCA: SVD($\mathbf{X}$)

PLS: SVD($\mathbf{X}'\mathbf{Y}$)

CCA: SVD($(\mathbf{X}'\mathbf{X}')^{-1/2}(\mathbf{X}'\mathbf{Y})(\mathbf{Y}'\mathbf{Y})^{-1/2}$)

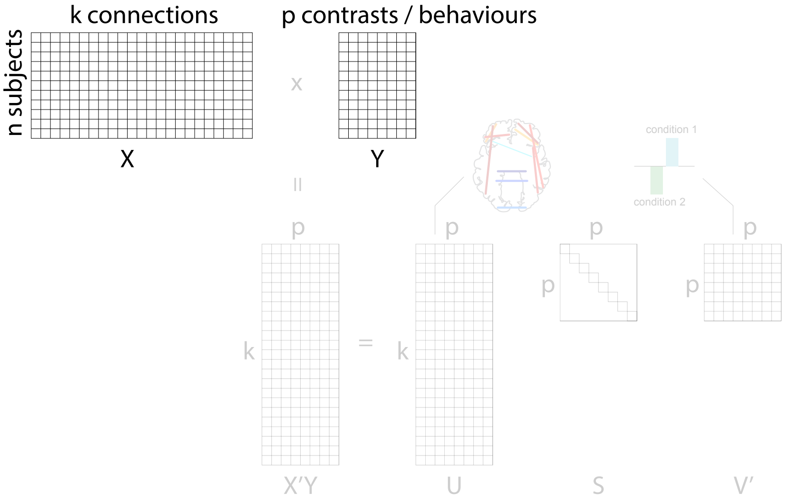


Worsley et al. (1997) *NeuroImage*

De Bie et al. (2005) *Handbook of Geometric Computing - Springer*

McIntosh & Mišić (2013) *Annu Rev Psychol*

Partial least squares (PLS)



Wold et al. (1982, 1984) *Mathematics and statistics in chemistry*

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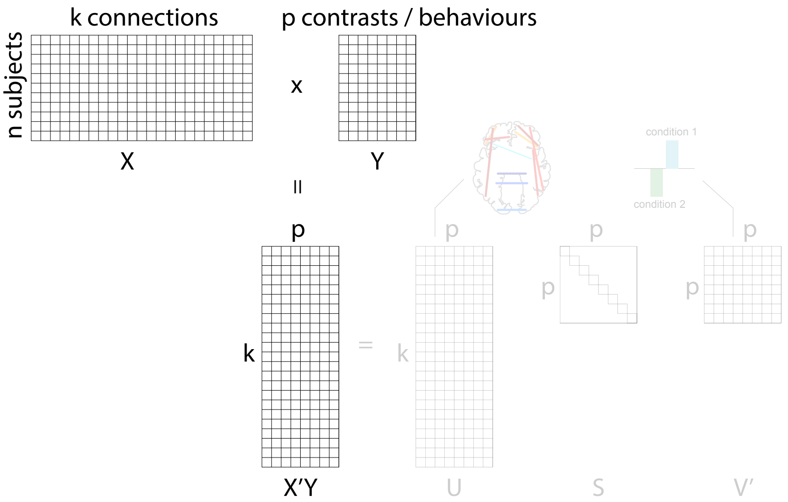

Wold et al. (1982, 1984) *Mathematics and statistics in chemistry*

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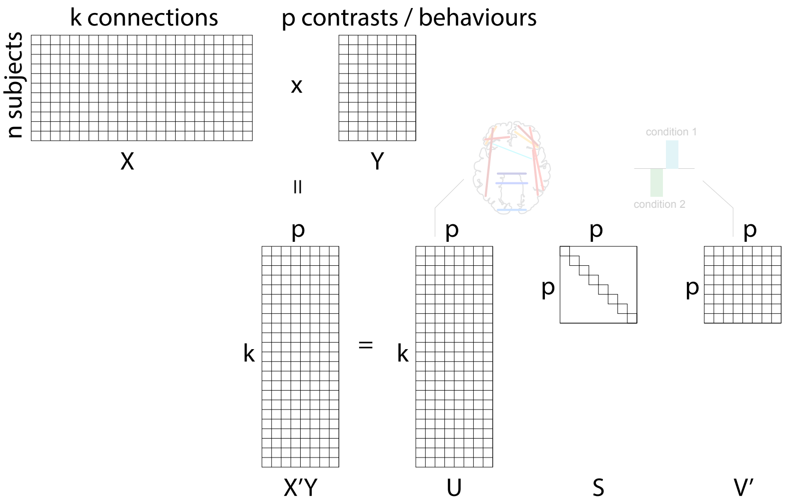

Wold et al. (1982, 1984) *Mathematics and statistics in chemistry*

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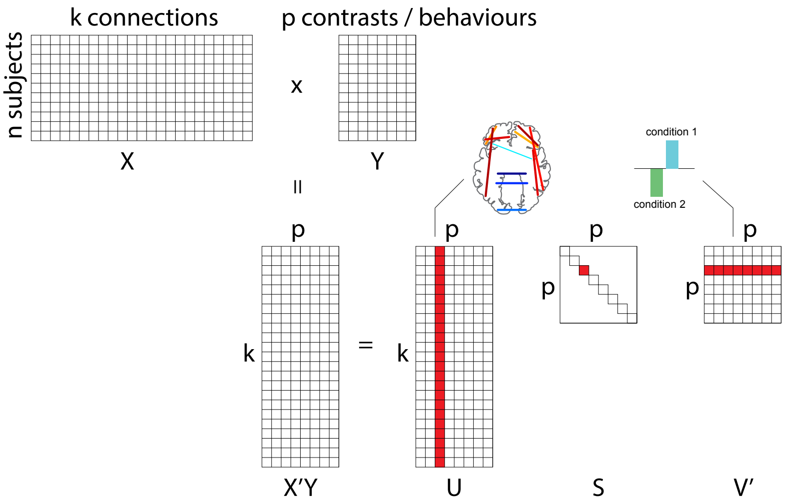
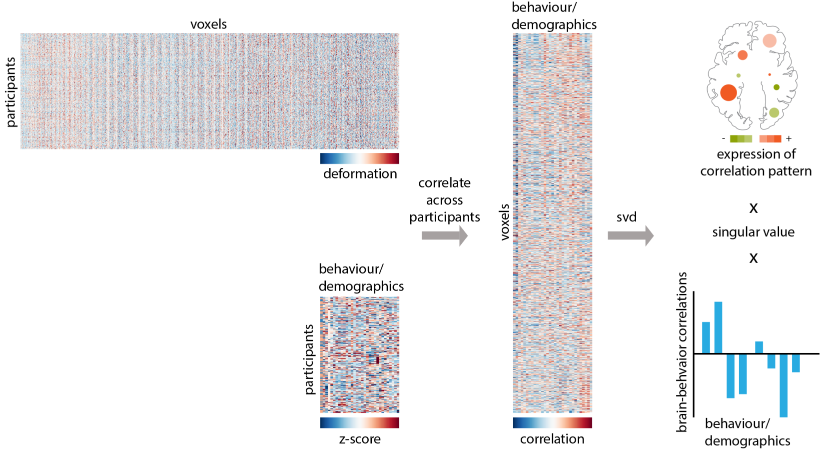


Wold et al. (1982, 1984) *Mathematics and statistics in chemistry*

Example: clinical-anatomical signature of Parkinson's



Zeighami et al. (2018) *NeuroImage*

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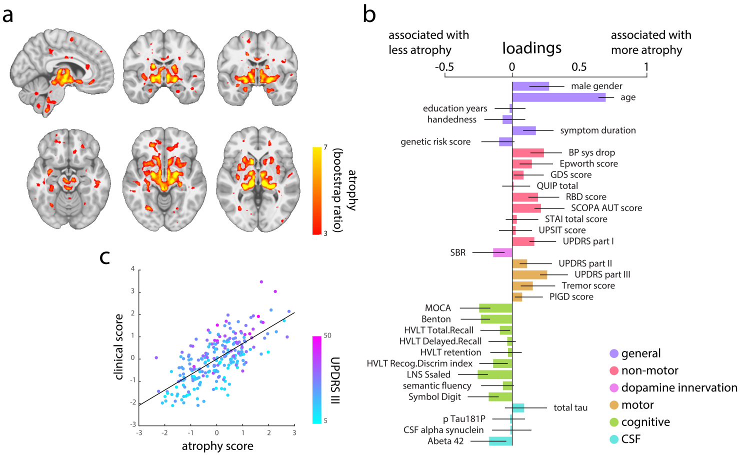


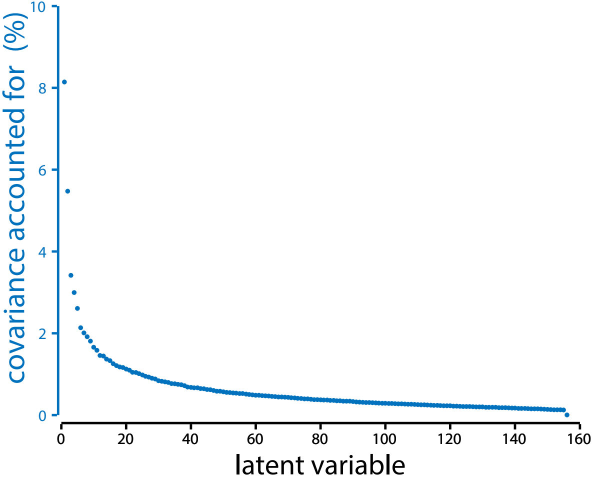
Zeighami et al. (2018) *NeuroImage*

Follow-up questions

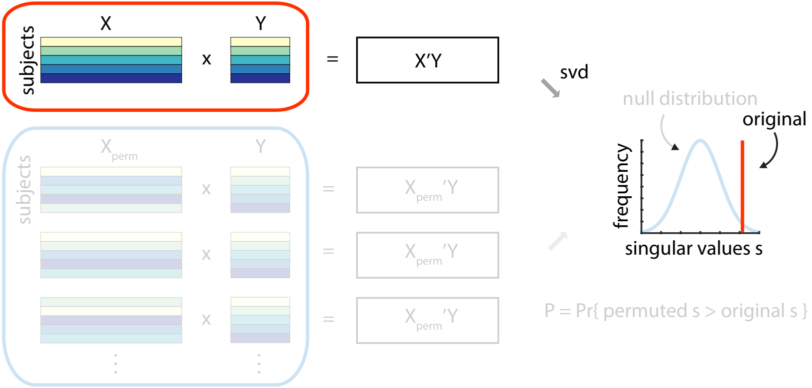
- which components are statistically meaningful?
- which variables are most important?
- how well to individual subjects express the multivariate pattern?

How many components to retain?

$$\% \text{ covariance} = s_i^2 / \sum_j s_j^2$$



Statistical significance: permutation tests



Edgington (1965, 1969) *J Psychol*

McIntosh et al. (1996, 2004) *NeuroImage*

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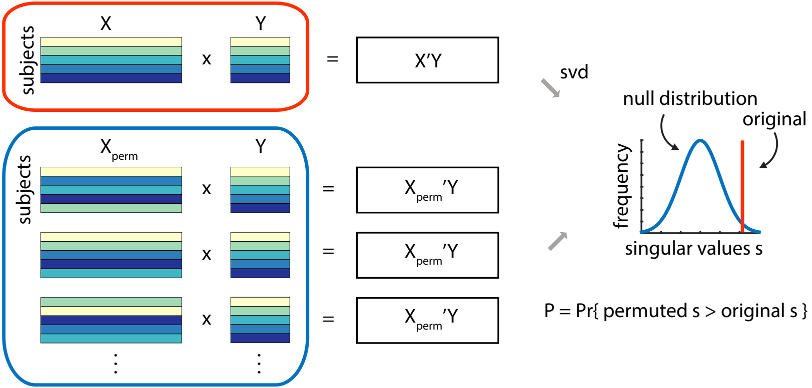
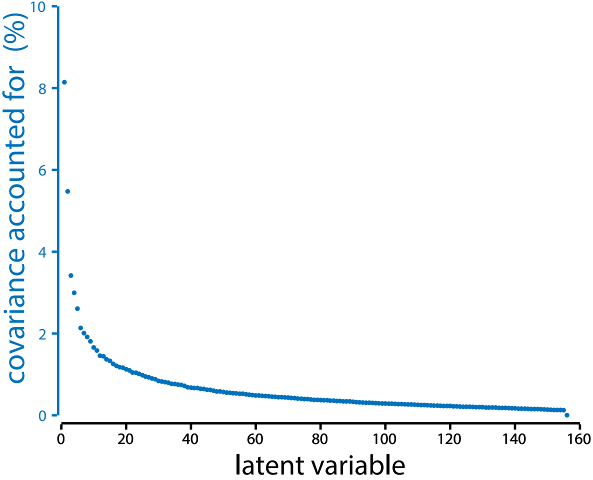


Edgington (1965, 1969) *J Psychol*

McIntosh et al. (1996, 2004) *NeuroImage*

How many components to retain?



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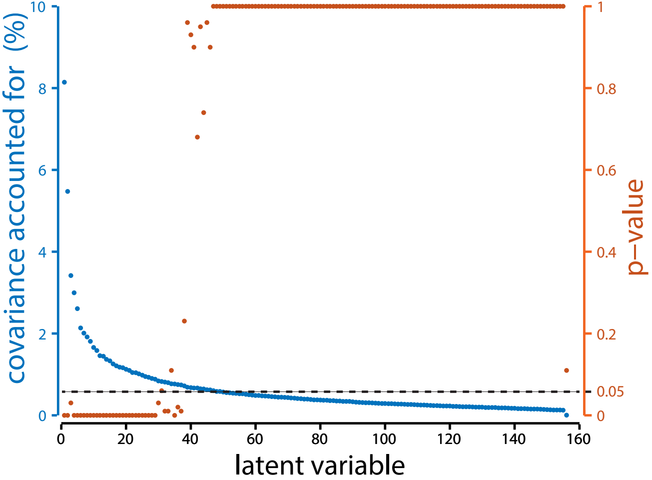

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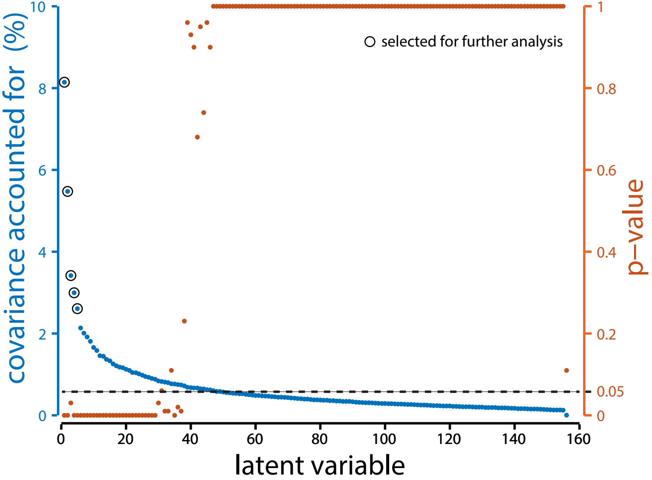
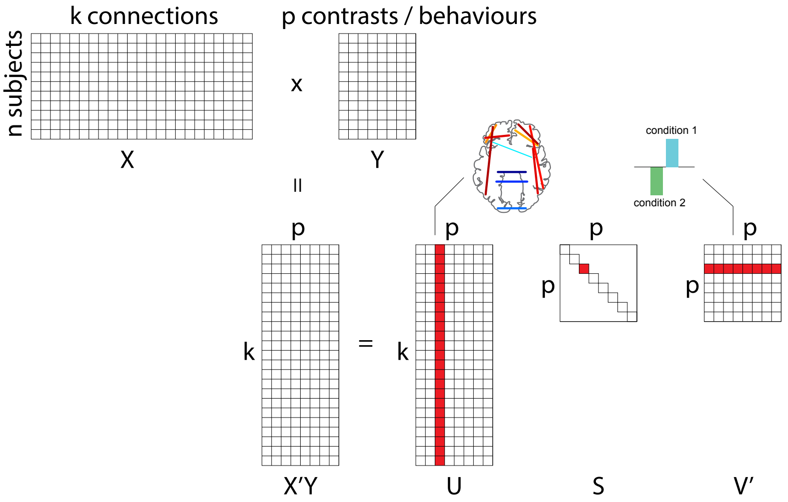
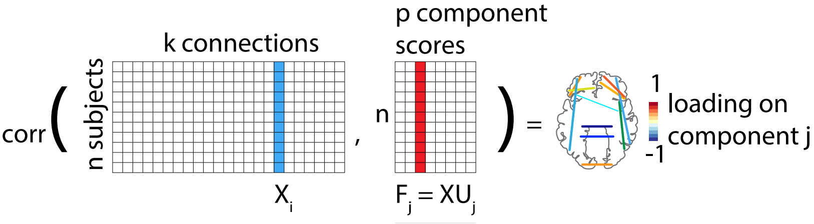


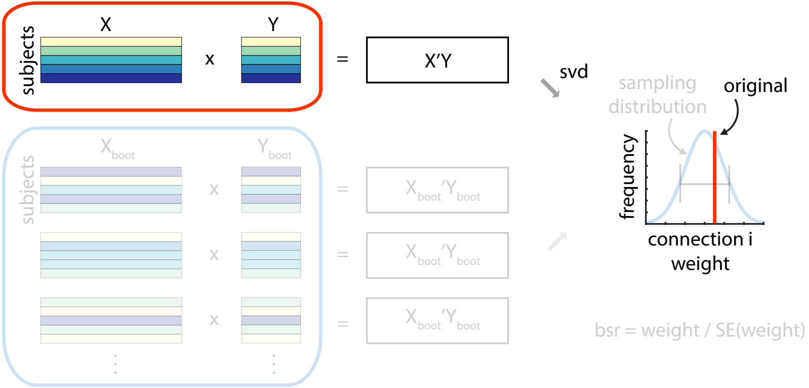
Which variables are important?



Shared variance: loadings



Reliability: bootstrapping



Efron & Tibshirani (1986) *Stat Sci*

McIntosh et al. (1996, 2004) *NeuroImage*

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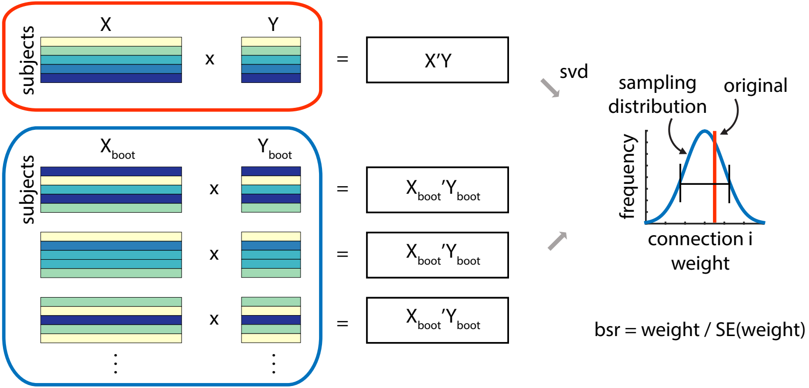
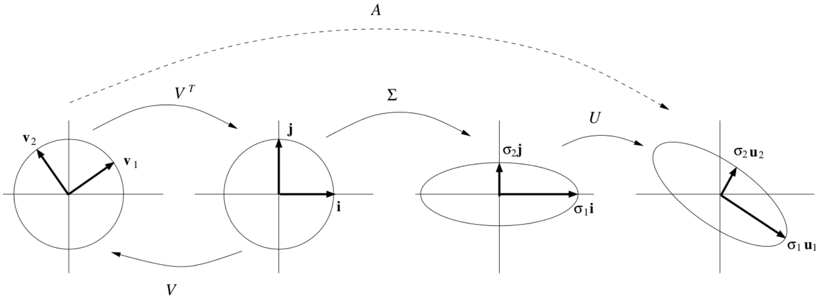


Efron & Tibshirani (1986) *Stat Sci*

McIntosh et al. (1996, 2004) *NeuroImage*

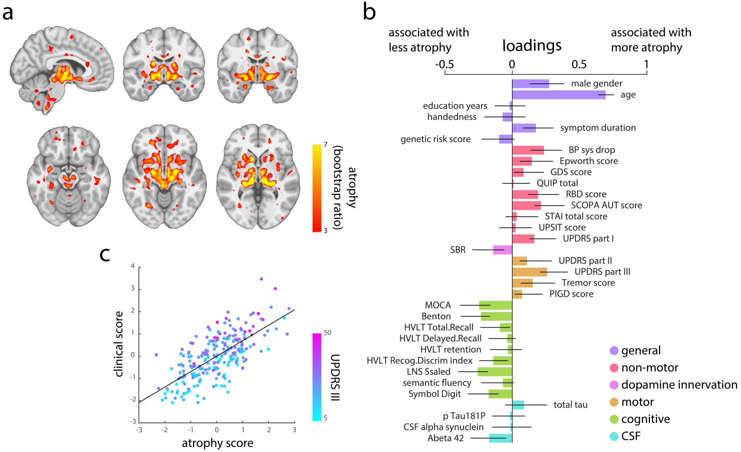
Matching randomized components

$$\mathbf{X}'\mathbf{Y} = \mathbf{USV}' \longleftrightarrow \mathbf{X}'_{\mathrm{boot}}\mathbf{Y} = \mathbf{U}_{\mathrm{boot}}\mathbf{S}_{\mathrm{boot}}\mathbf{V}'_{\mathrm{boot}}$$



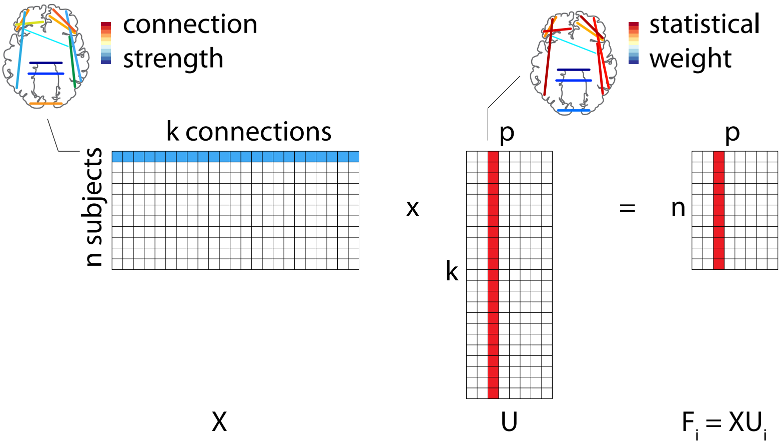
Milan & Whittaker (1995) *J Roy Stat Soc C*

Example: clinical-anatomical signature of Parkinson's

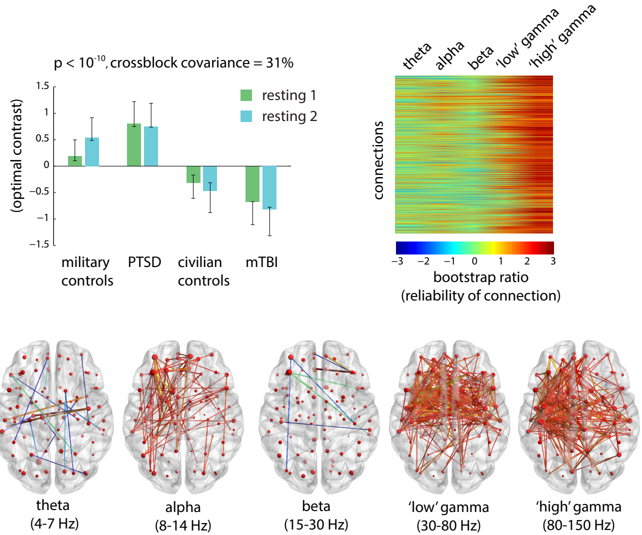


Zeighami et al. (2018) *NeuroImage*

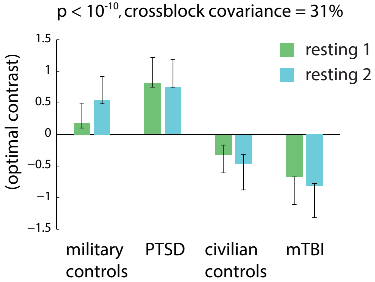
Individual participants

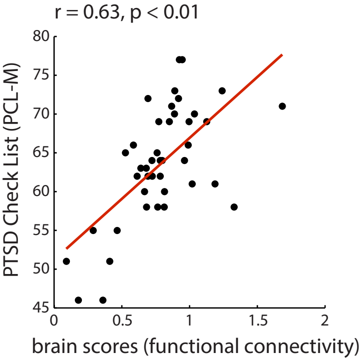


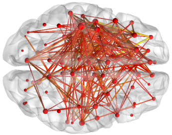
Example: connectivity differentiates PTSD from mTBI



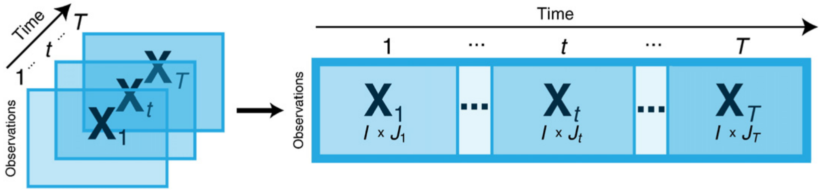
Example: connectivity and symptom severity in PTSD





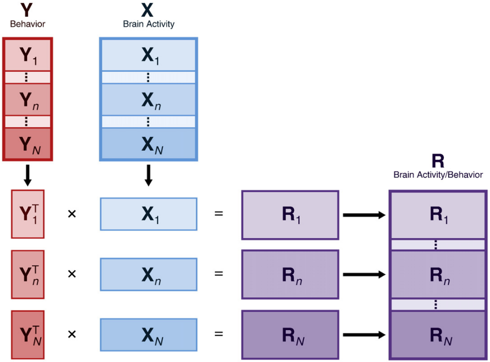


Adding other dimensions



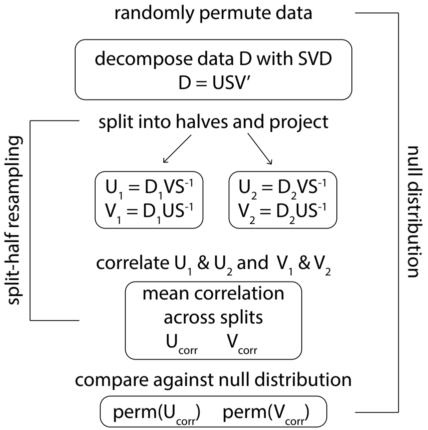
Krishnan et al. (2011) *NeuroImage*

Adding other dimensions



Krishnan et al. (2011) *NeuroImage*

Cross-validation: split-half resampling

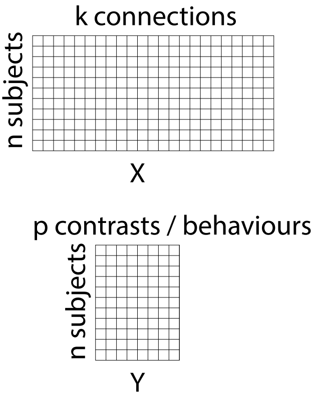


Strother et al. (2002) *NeuroImage*

Kovacevic et al. (2013) *New perspectives in Partial Least Squares* (Ed: Abdi)

Canonical correlation analysis (CCA)

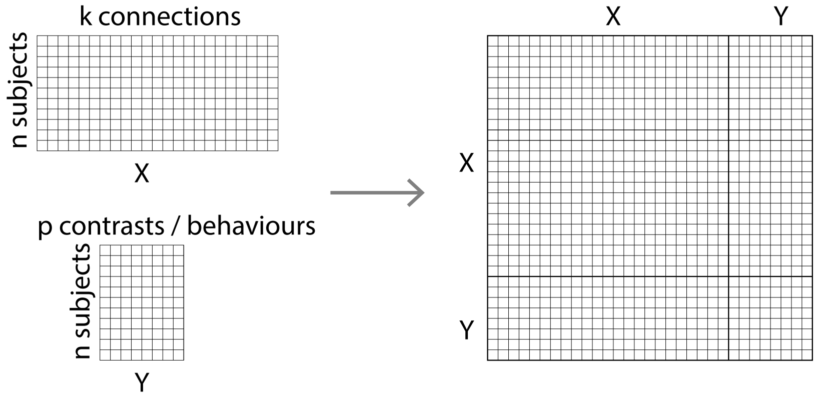
$$\mathrm{SVD}((\mathbf{X}'\mathbf{X}')^{-1/2}(\mathbf{X}'\mathbf{Y})(\mathbf{Y}'\mathbf{Y})^{-1/2})$$



Hotelling (1936) *Biometrika*

Canonical correlation analysis (CCA)

$$\text{SVD}((\mathbf{X}'\mathbf{X}')^{-1/2}(\mathbf{X}'\mathbf{Y})(\mathbf{Y}'\mathbf{Y})^{-1/2})$$



Hotelling (1936) *Biometrika*

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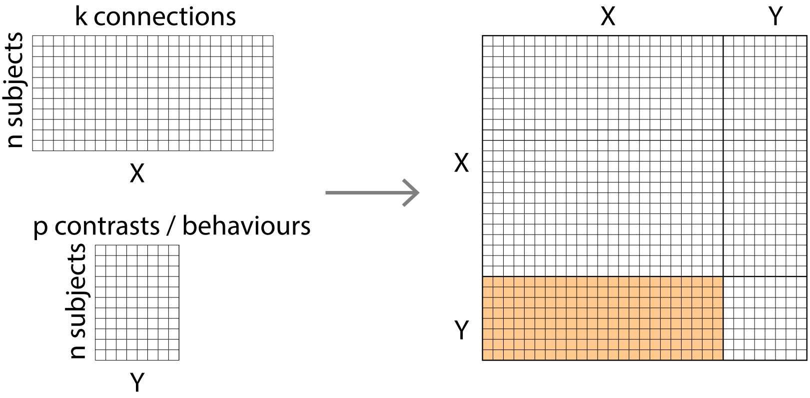

Hotelling (1936) *Biometrika*

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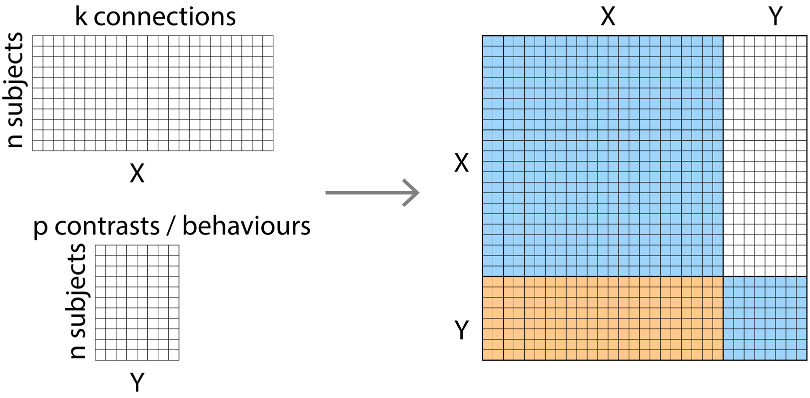
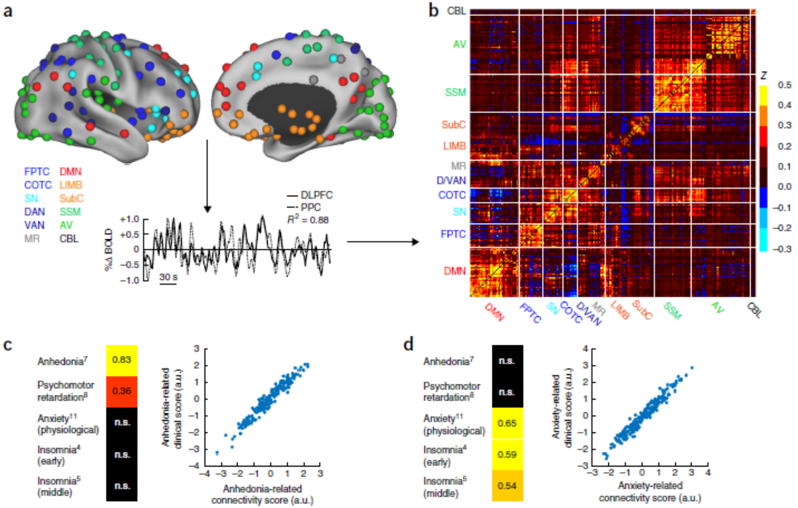


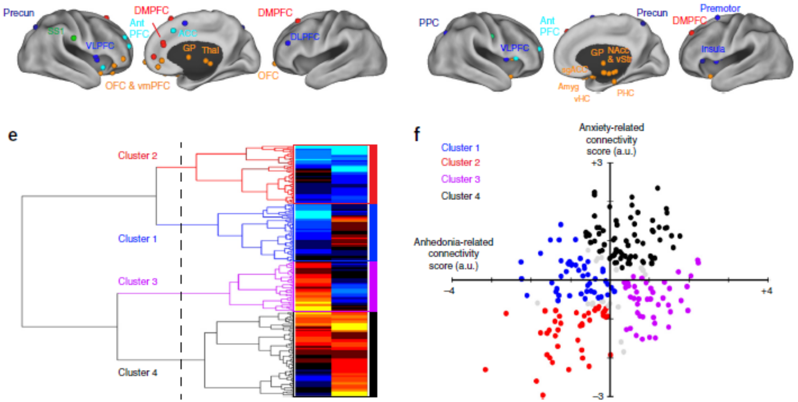
Hotelling (1936) *Biometrika*

Behaviour- and connectivity-defined subtypes of depression



Drysdale et al. (2016) *Nat Med*

Behaviour- and connectivity-defined subtypes of depression



Drysdale et al. (2016) *Nat Med*

Linear discriminant analysis (LDA)

- LDA: maximize between- vs. within-group variance
- SVD($\mathbf{W}^{-1}\mathbf{B}$)

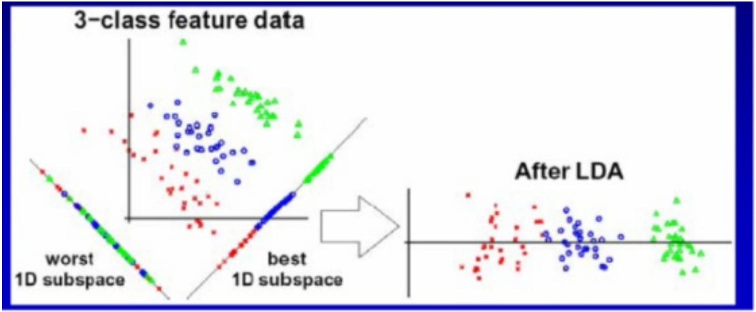


image: https://mlalgorithm.wordpress.com/

Friston et al. (1995) *NeuroImage*

Extensions

- sparse/regularized solutions, e.g.
  sCCA: Witten & Tibshirani (2009) *Stat Appl Genet Mol Biol*
  PLS-CA: Beaton et al. (2015) *Psychol Meth*
- extensions to 3+ data sets, e.g.
  PARAFAC: Bro (1997) *Chemometr Intell Lab*
  Multiway PLS: Wold et al. (1987) *J Chemometrics*
- nonlinear dependencies
- Bayesian implementations, e.g.
  IBFA: Virtanen et al. (2011) *ICML-II*
- prediction

Limitations and considerations

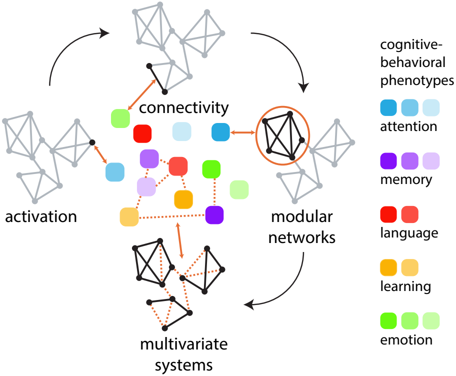
- overfitting
- linear
- unique partitioning of variance/covariance
- inference on individual variables

Resources

- Matlab toolbox for dimensionality reduction
  https://lvdmaaten.github.io/drtoolbox/
- PLS toolbox
  https:
  //www.rotman-baycrest.on.ca/index.php?section=84
- sparse CCA
  http://statweb.stanford.edu/~tibs/Correlate/

Summary

- multivariate models embody network property
- all techniques entail unique assumptions
- many linear multivariate techniques are related
- multivariate techniques are versatile



Demo: *MyConnectome*

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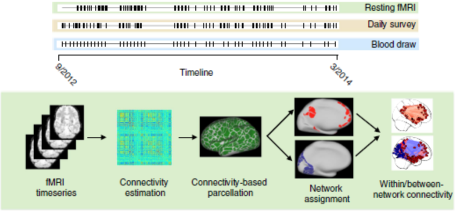
Long-term neural and physiological phenotyping of a single human

Russell A. Poldrack[1,2,3,4], Timothy O. Laumann[5], Oluwasanmi Koyejo[4], Brenda Gregory[3], Ashleigh Hover[3], Mei-Yen Chen[1], Krzysztof J. Gorgolewski[4], Jeffrey Luci[2,3], Sung Jun Joo[1], Ryan L. Boyd[1], Scott Hunicke-Smith[6], Zack Booth Simpson[7], Thomas Caven[8], Vanessa Sochat[9], James M. Shine[4], Evan Gordon[5], Abraham Z. Snyder[5], Babatunde Adeyemo[5], Steven E. Petersen[5], David C. Glahn[10,11], D. Reese Mckay[10,11], Joanne E. Curran[12], Harald H.H. Göring[13], Melanie A. Carless[13], John Blangero[12], Robert Dougherty[14], Alexander Leemans[15], Daniel A. Handwerker[16], Laurie Frick[3], Edward M. Marcotte[7,17] & Jeanette A. Mumford[1]



Poldrack et al. (2015) *Nat Commun*