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Machine Learning I: basics

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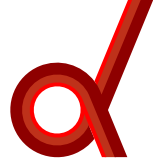
Machine Learning and Pattern Recognition

- Pattern Recognition (PR) is a subfield of machine learning, which relates to the automatic discovery of patterns of statistical regularity in data
- Aim to learn from empirical data rather than following fixed rules
- **Learn by example**
- Increasingly used in computational psychiatry for:
  1. Predicting clinical variables (diagnosis or treatment response)
  2. Stratifying psychiatric disorders
  3. Learning mappings between behaviour and brain systems

Outline



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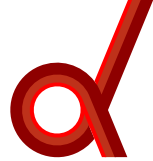


What is pattern recognition used for?

Historically, has been applied in many application domains:

Example Applications

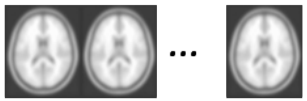
- Speech Recognition
- Automatic Character recognition / handwriting recognition
- Document classification (e.g. spam filters)
- Analysis of genetic microarray data
- Self-driving cars
- Recommender systems / online shopping
- ...

Types of pattern recognition

Supervised learning involves learning a mapping between input and output:

Input

Training examples
$\{x_1, x_2, ..., x_N\}$



Output

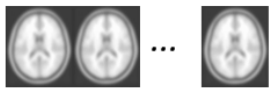
Target variables
$\{y_1, y_2, ... y_N\}$

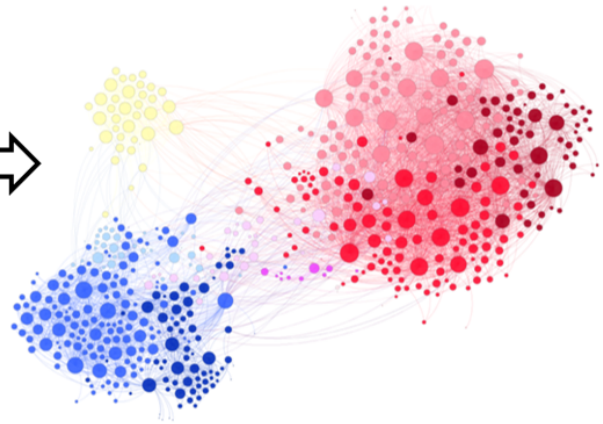
$y_i \in R$: regression
$y_i \in \{0,1\}$: classification

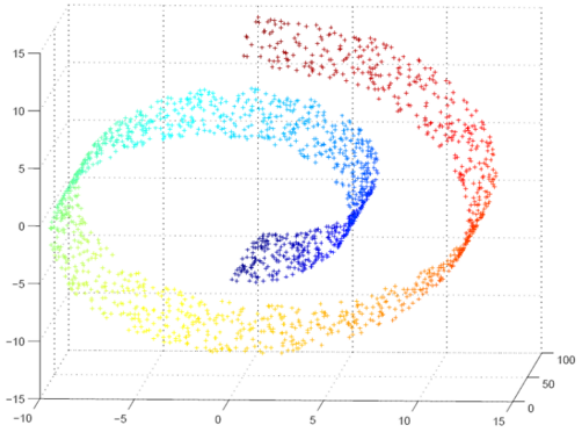
In **Unsupervised** learning, algorithms are not provided with output labels and must learn to structure the data by applying heuristics

Input

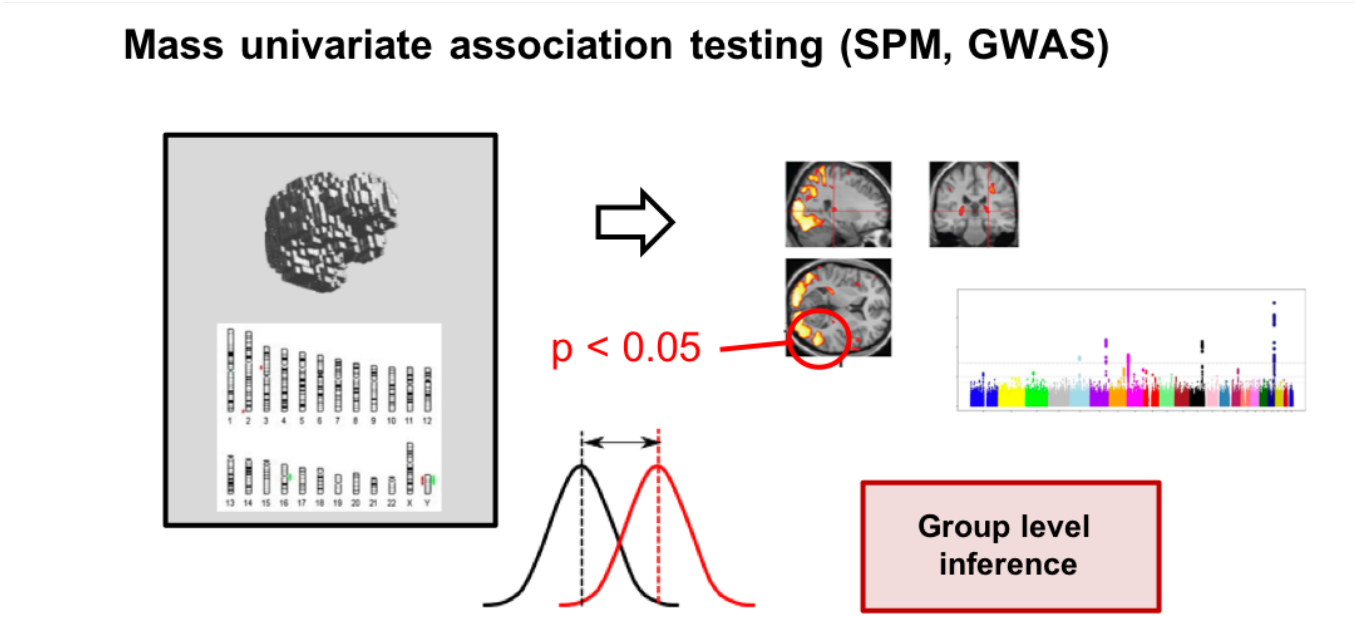
Training examples
$\{x_1, x_2, ..., x_N\}$







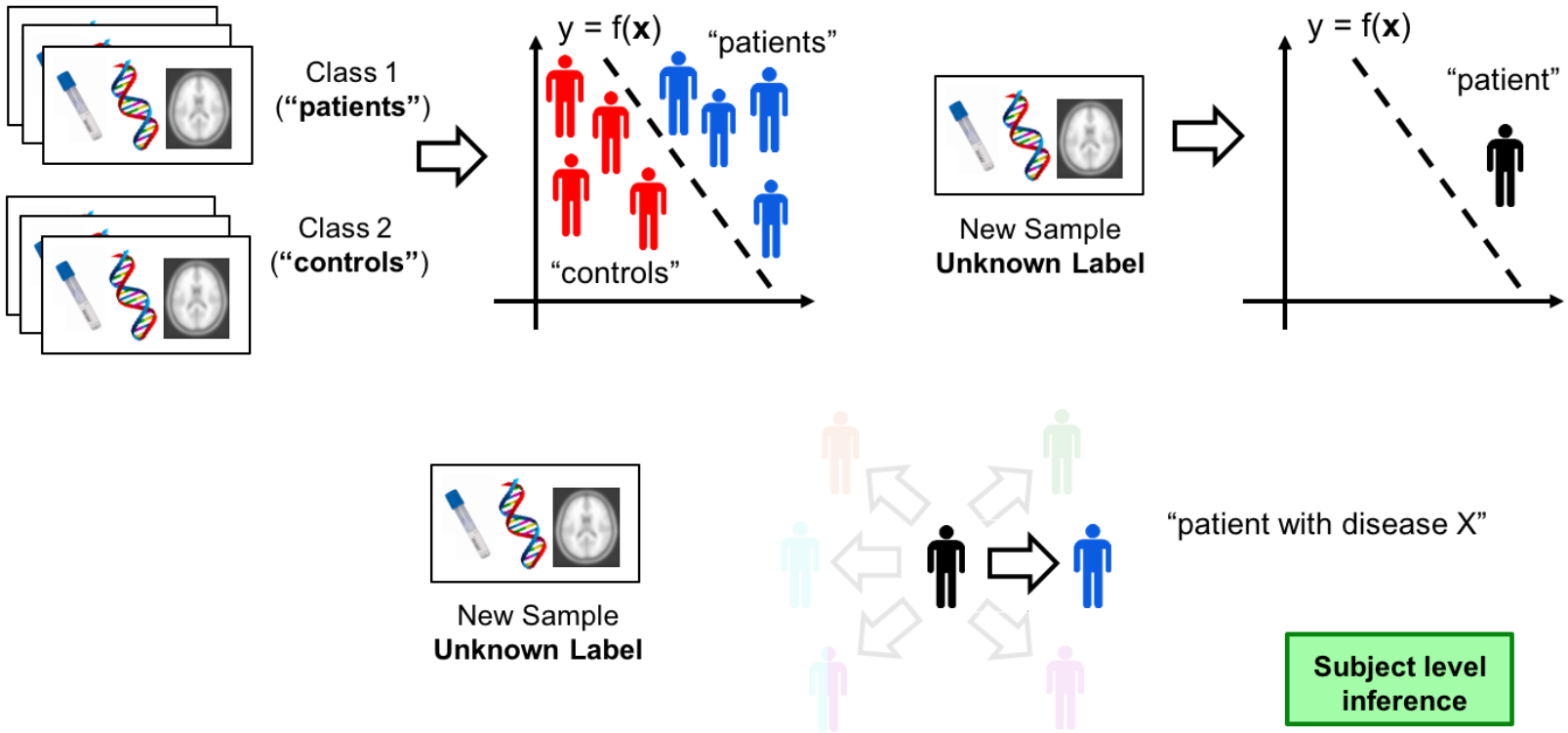
Biomarkers for prediction



- Useful for understanding mechanisms
- For clinical decision making this does not suffice. It is necessary to make predictions about individuals

Predicting disease state

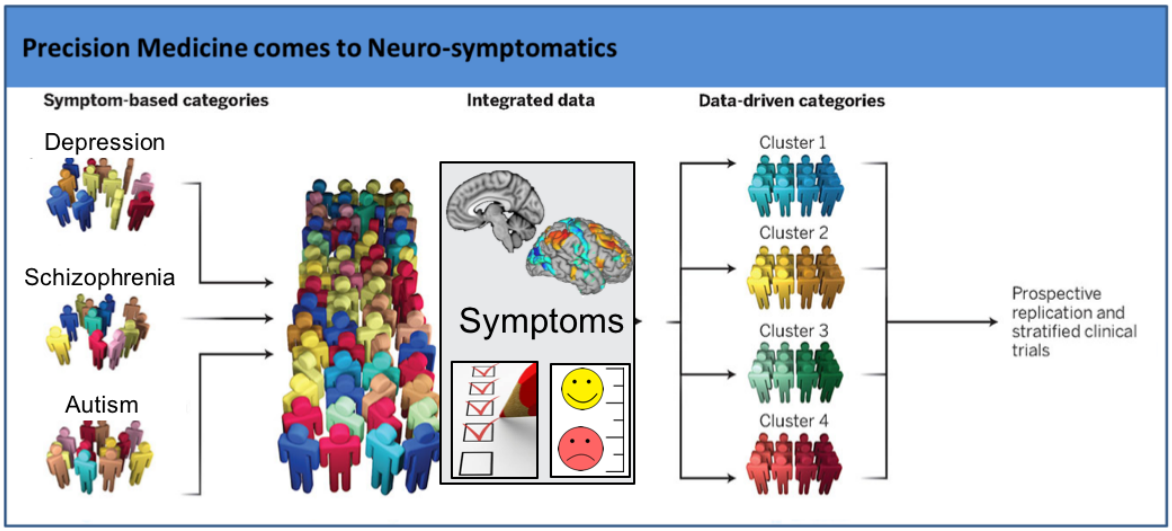
Making subject level predictions of diagnosis and outcome



Useful to find a measure of overall group separation

Machine Learning in Psychiatry: Stratification

Tackling the clinical and biological heterogeneity of psychiatric disorders

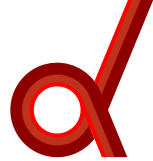


NIH National Institute of Mental Health

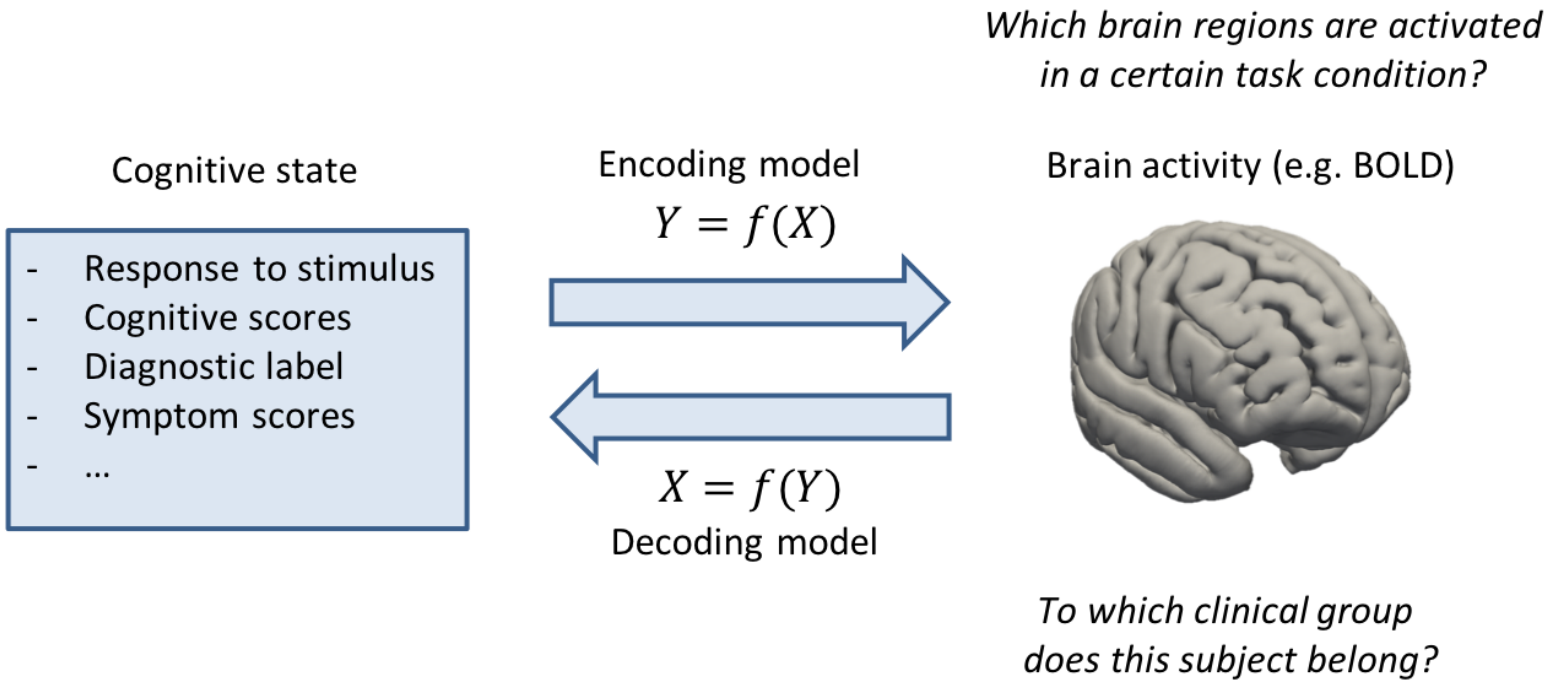
RDoC Research Domain Criteria Initiative

Insel et al. (2015)

Outline



Encoding and Decoding

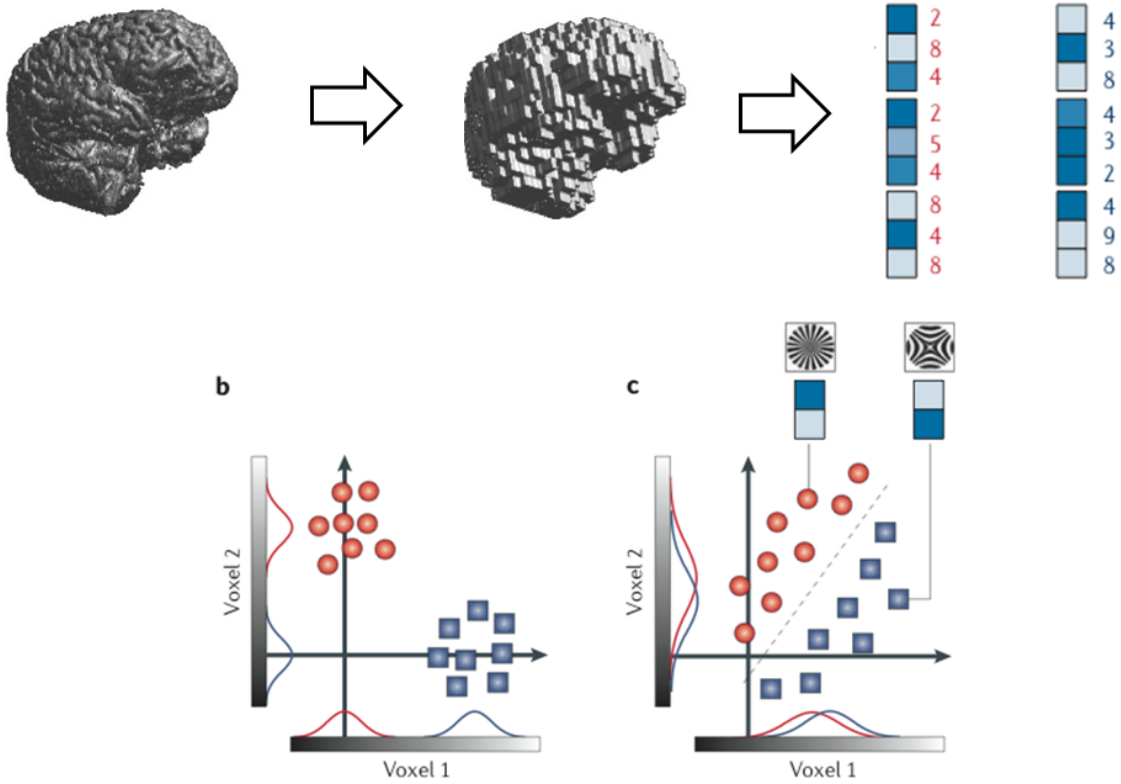


- Also called Generative/Recognition models
- $\neq$ Generative/Discriminative models in machine learning
- This distinction relates to the brain, not to the methods

Naselaris et al. (2011)

Multivariate models

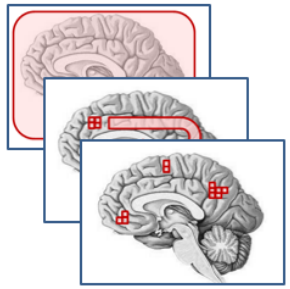
Sensitivity for spatially distributed (or multivariate) effects:



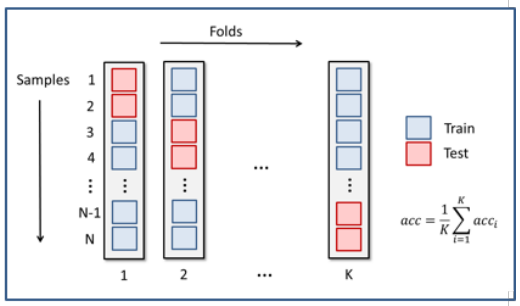
Haynes and Rees (2006)

Stages of supervised pattern recognition analysis

1. Feature extraction and/or feature selection

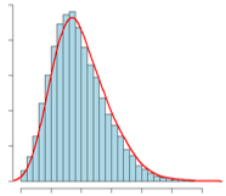


2. Classification / Regression using cross-validation

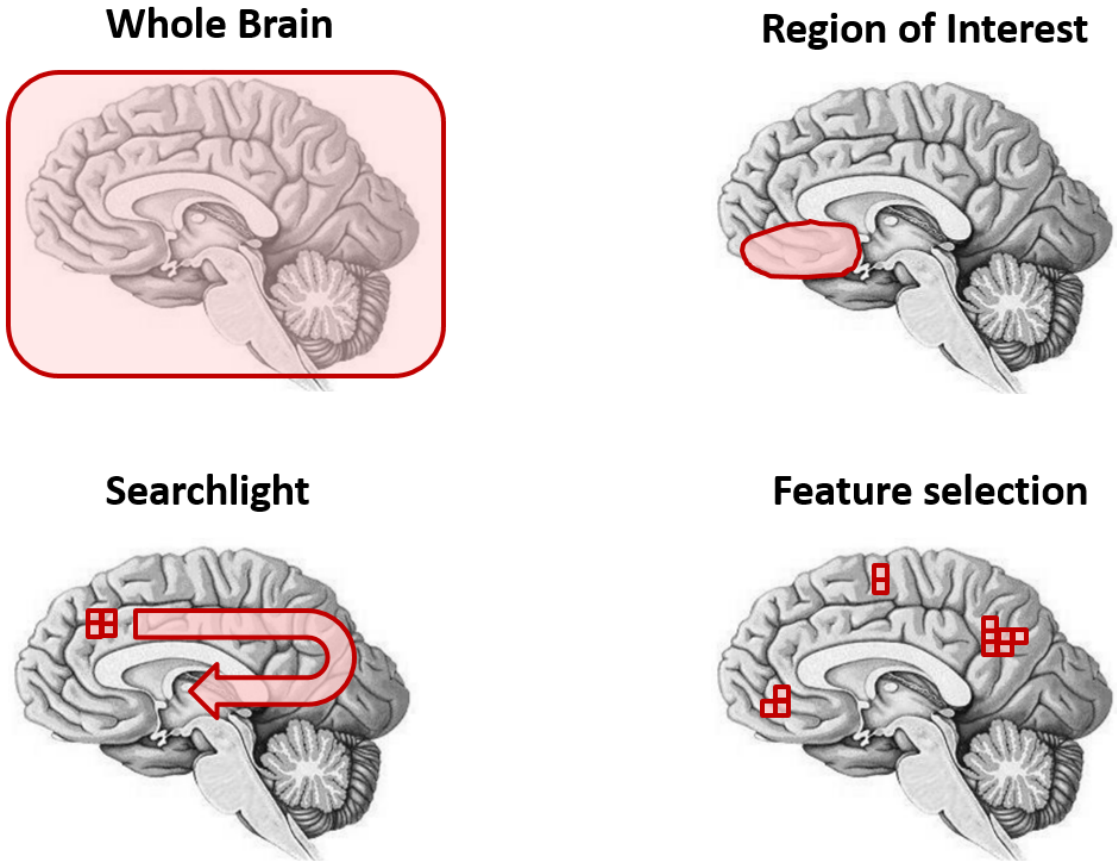


3. Performance evaluation

$$acc = \frac{1}{K}\sum_{i=1}^{K} acc_i$$



Feature selection and feature construction



- Can also construct features (e.g. using ICA/ PCA,...)
- Or learn features from the data (e.g. deep learning)
- Feature selection should be performed on training data only!

Notation

$\mathcal{D} = \{\boldsymbol{X}, \boldsymbol{y}\}$ or $\{\boldsymbol{X}, \boldsymbol{Y}\}$	Dataset
$\boldsymbol{X}_{N \times D} = [\boldsymbol{x}_1, ..., \boldsymbol{x}_N]^T$	N samples, D features
$\boldsymbol{y} = [y_1, ..., y_N]^T$	Targets
$\boldsymbol{w} = [w_1, ..., w_D]^T$	Weights

Approaches to Supervised Pattern Recognition

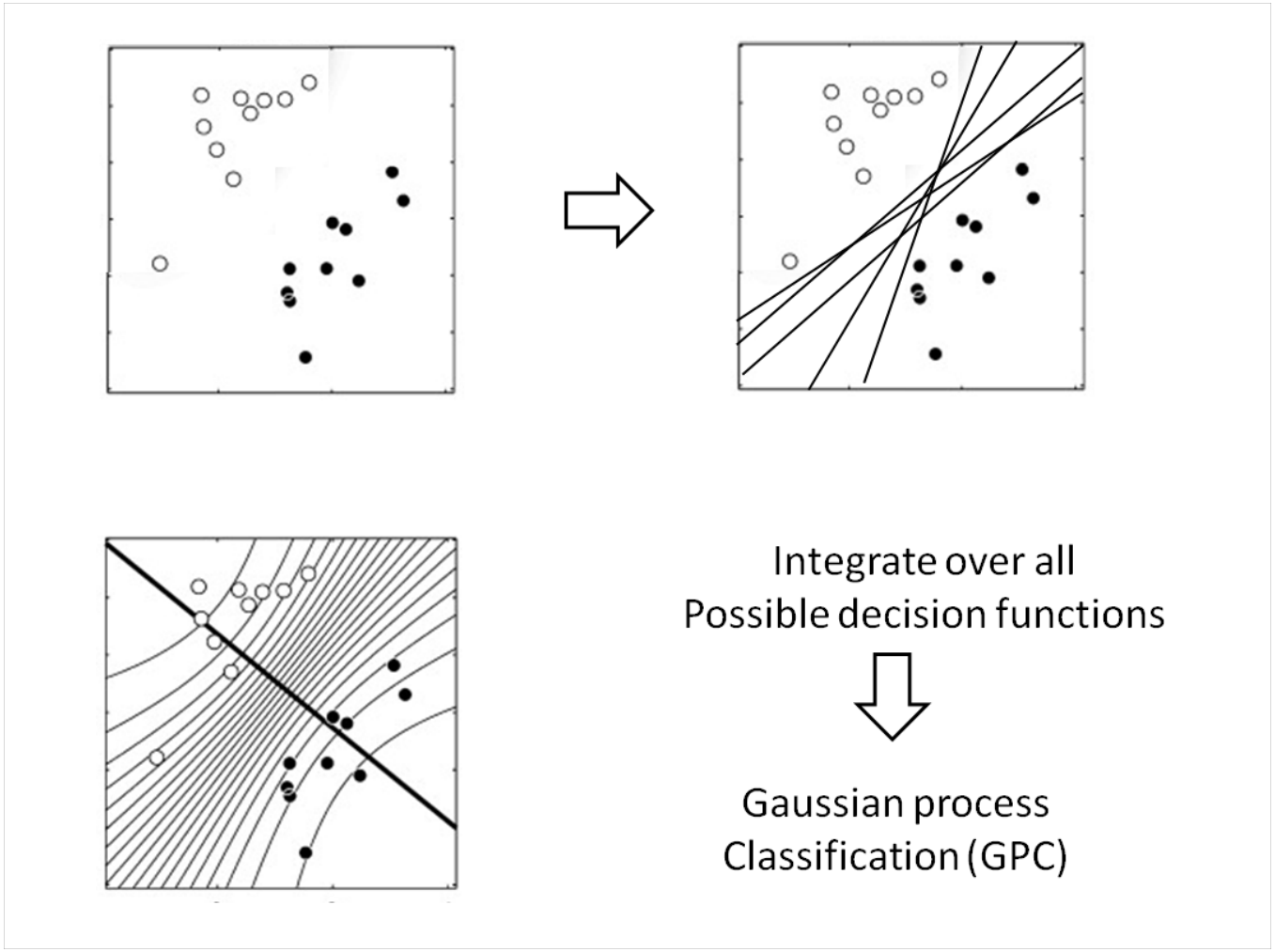
A smorgasbord of different approaches

- Regularisation methods (Penalized linear models, support vector machines, ...)
- Probabilistic approaches (Linear discriminant analysis, Gaussian processes, ...)
- Ensemble methods (Random forests, boosting, ...)
- Neural networks (multi-layer perceptrons, deep learning, ...)

Most methods aim to trade-off data fit with complexity

$$
\begin{aligned}
f(\boldsymbol{x}_i, \boldsymbol{w}) = f_i = \boldsymbol{x}_i^T \boldsymbol{w} \quad & \Rightarrow \hat{\boldsymbol{w}} = \min_w \sum_{i=1}^{n} \ell(y_i, f_i) + \lambda J(\boldsymbol{w}) \\
& \Rightarrow \hat{\boldsymbol{w}} = \min_{\mathrm{w}} - \ln p(\boldsymbol{w}|\boldsymbol{y}) \\
& = \min_{\mathrm{w}} \sum_{i=1}^{n} \ln p(y_i|f_i) + \ln p(\boldsymbol{w}|\boldsymbol{\theta})
\end{aligned}
$$

Choice of pattern recognition algorithm

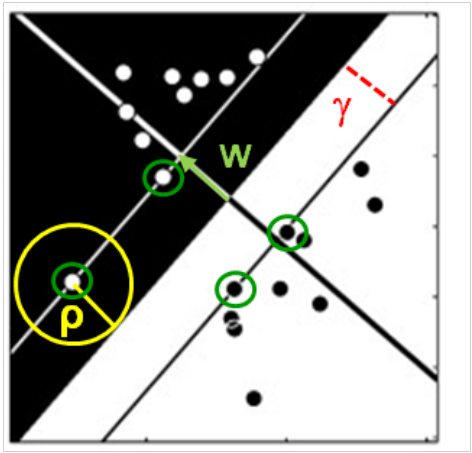


All methods make assumptions!

Ashburner and Klöppel (2011)

Support Vector Machines

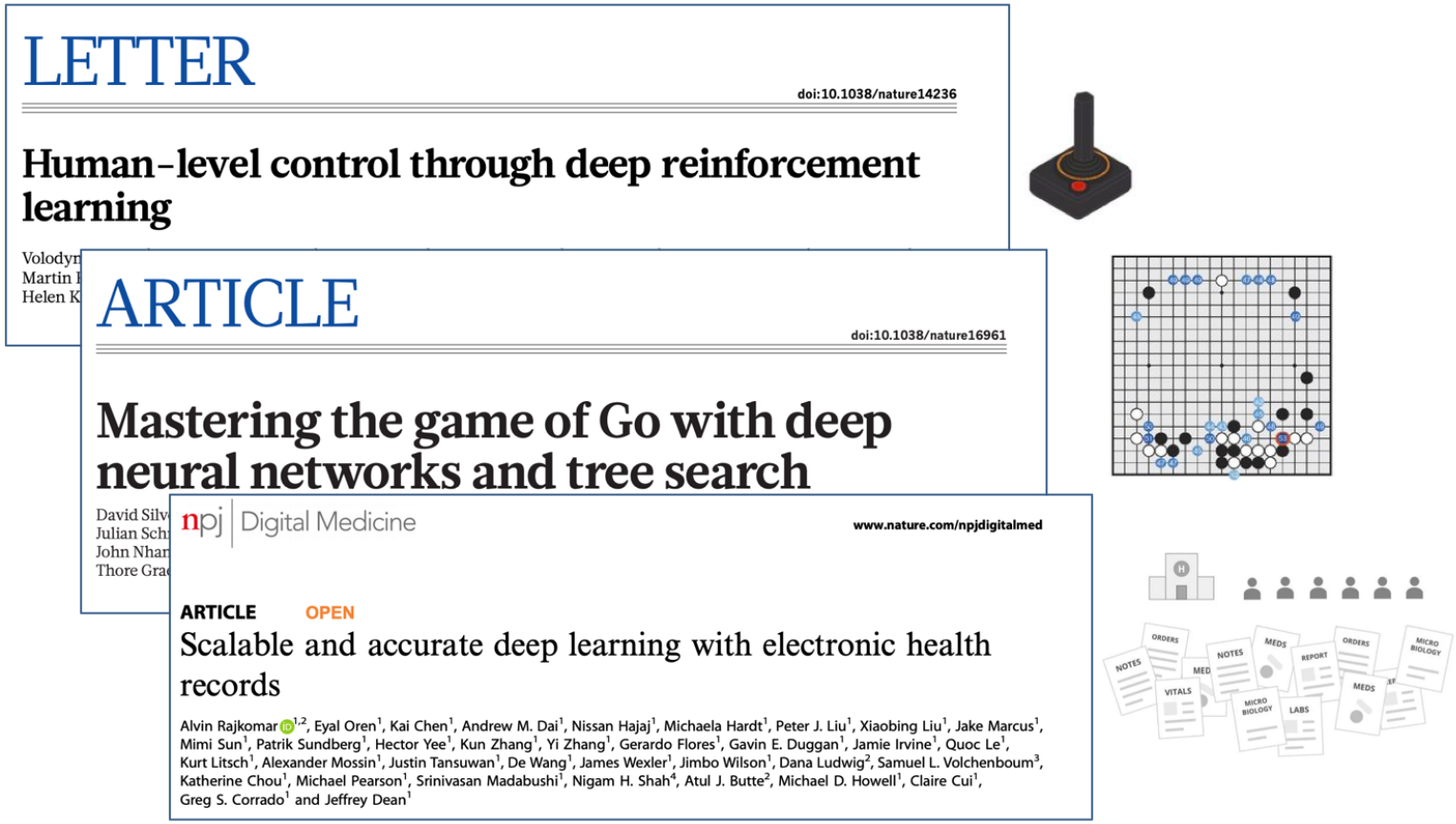
- Finds a separating hyperplane that is "optimal" in that it leads to the largest margin between classes (γ)
- Based on the assumption that each point is bounded by unknown noise (ρ)
- New points will be well classified if $\gamma > \rho$
- The hyperplane is uniquely defined by a subset of the most ambiguous data points ("support vectors")



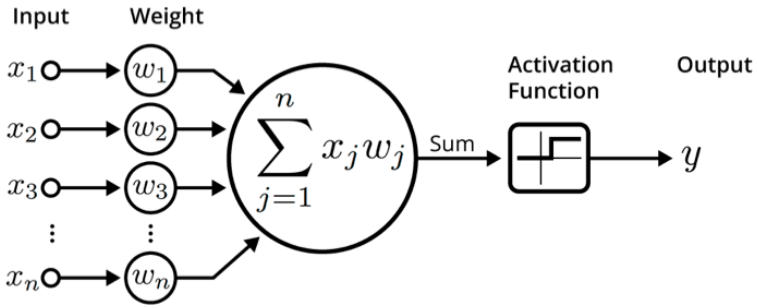
$$\begin{aligned} \min_{w,\xi,b} \quad & -\gamma + C\sum_{i=1}^{N}\xi_i \\ \text{s.t.:} \quad & y_i(\boldsymbol{w}^T\phi(\boldsymbol{x}) + b) > \gamma - \xi_i \\ & \xi_i > 0 \\ & ||\boldsymbol{w}||^2 = 1 \end{aligned}$$

Deep Learning

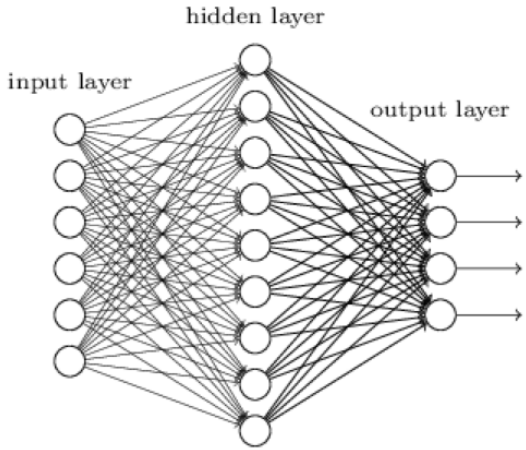
- 'Deep' neural networks have seen an enormous surge in popularity over the last few years
- Extend 1950s-era neural networks to have many hidden layers
- Now provide state of the art performance in many domains, e.g. computer vision, game playing and perception



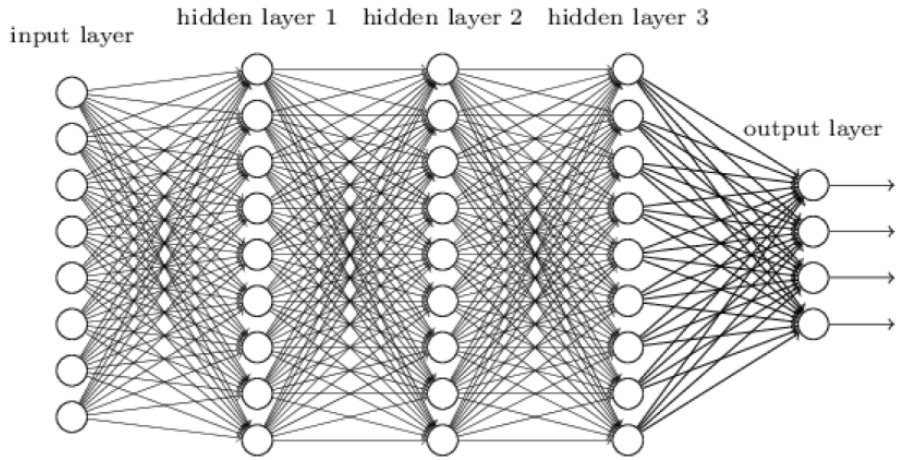
Deep Learning



"Non-deep" feedforward neural network



Deep neural network



- Many variants but "convolutional" networks are popular
- Predominantly supervised learning
- Usually many parameters to optimise (more in lecture 2)

Deep Learning

ImageNet Classification with Deep Convolutional Neural Networks

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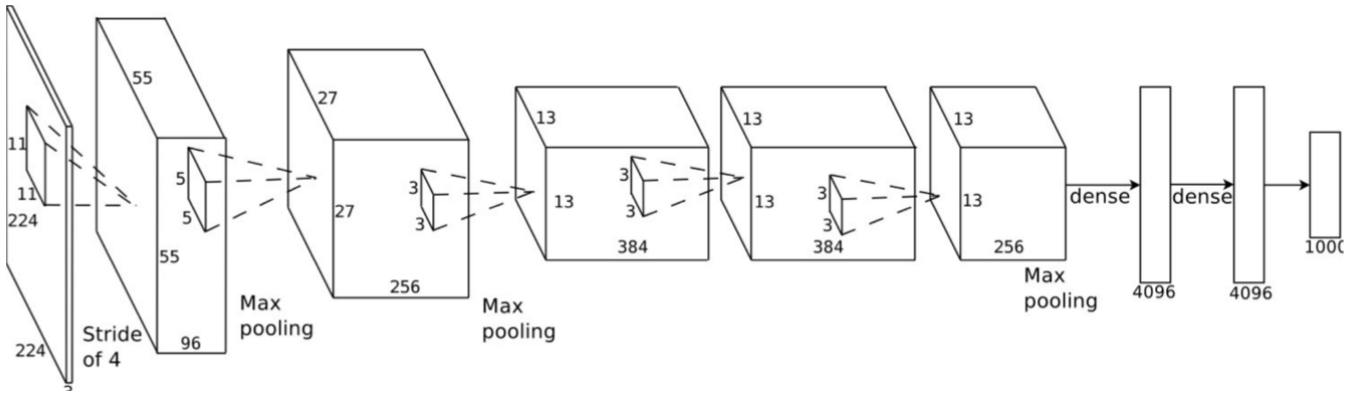
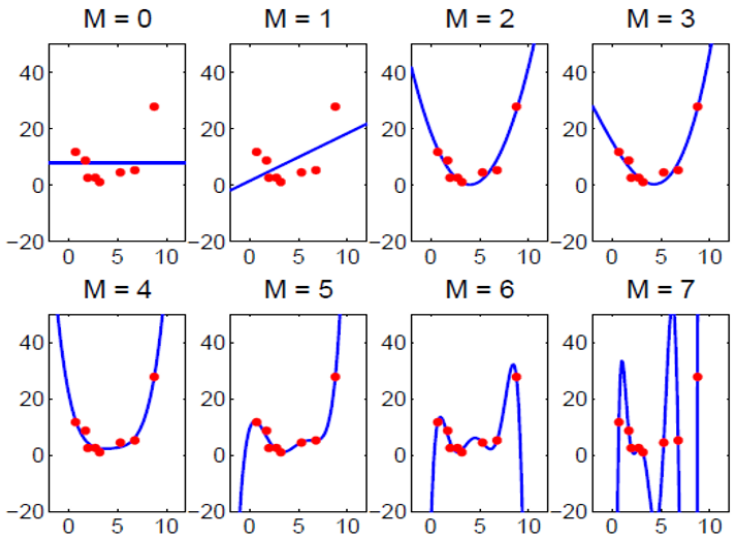
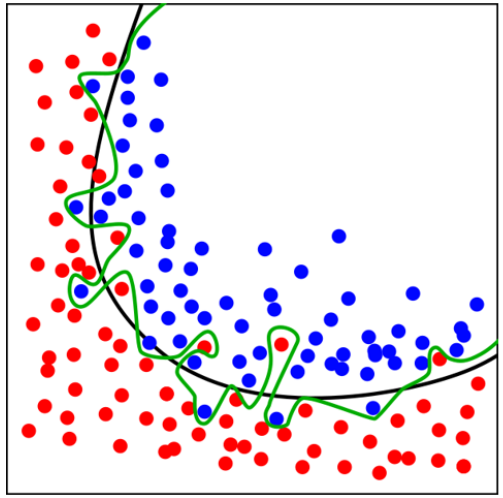


- 7 layer network that won 2012 ImageNet large-scale visual recognition challenge by 10%
- Trained the network on 15 million annotated images from over 22,000 categories
- more than 93,000 citations since 2012!

Overfitting

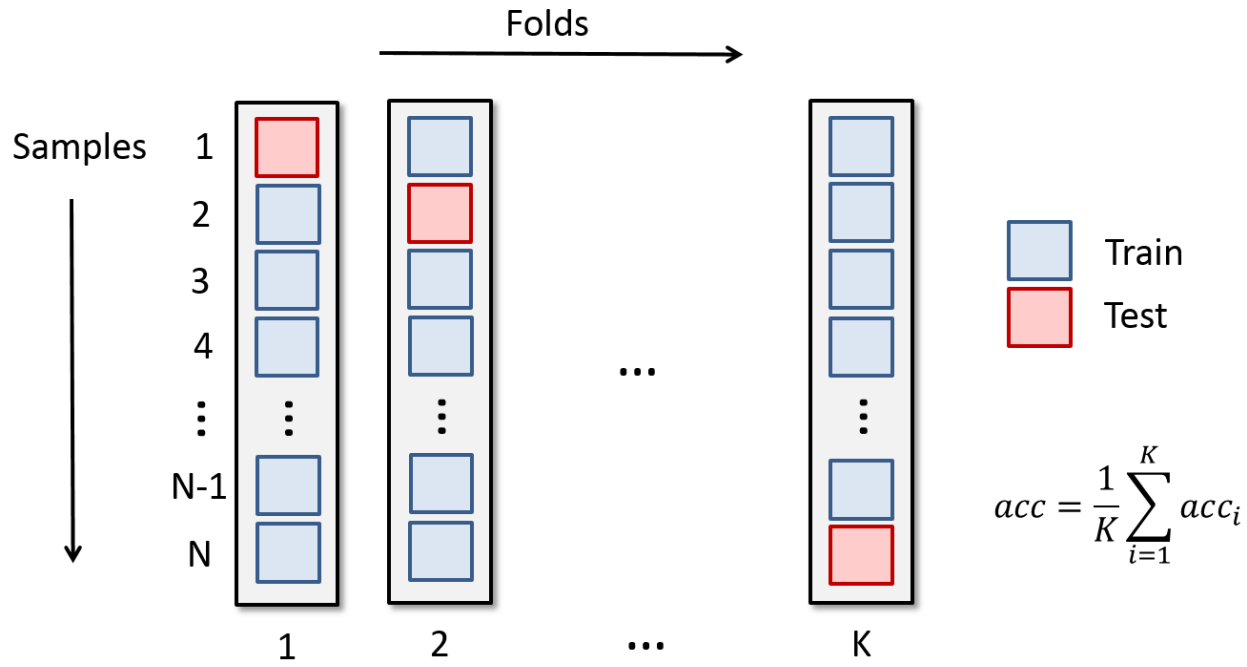
- Occurs when an model performs well on the data that it was estimated or trained on, but poorly on new data
- Can arise in very many ways including improper parameter optimisation or feature selection





Cross-validation

- Testing on unseen data is essential to assess generalizability
- Cross-validation one popular way to do this
- 'K-fold CV': split the data into K approximately equal chunks
- 'Leave-one-out': one sample is left out at at a time ($K = N$)

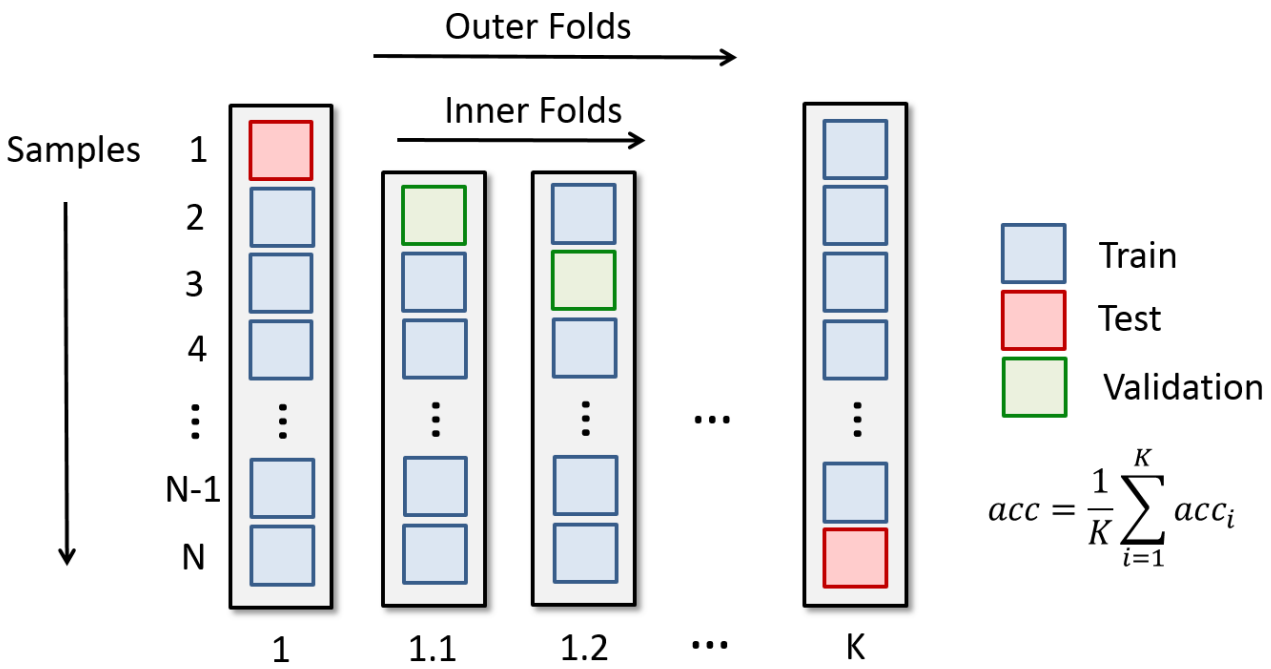


Parameter optimisation

- Most approaches depend on multiple (hyper)parameters
- e.g. regularization parameters in penalized linear models

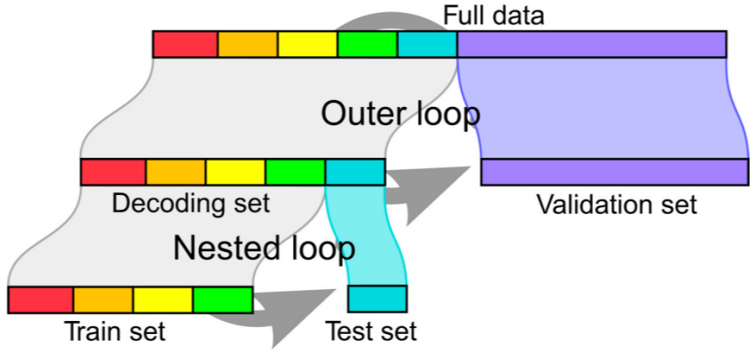
$$\hat{\boldsymbol{w}} = \min_w \sum_{i=1}^{n} \ell(y_i, f_i) + \lambda J(\boldsymbol{w})$$

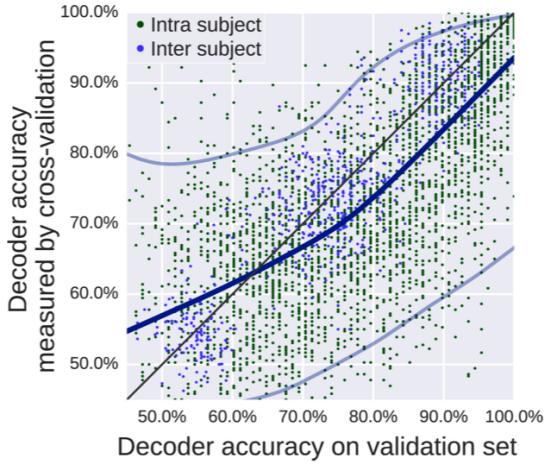
- Standard approach is *nested* cross-validation with a grid search

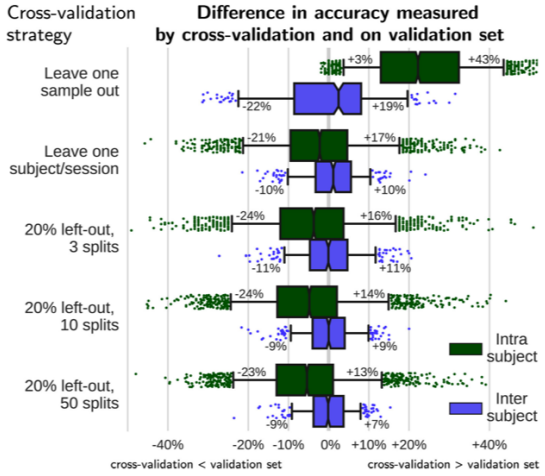


Multi-stage validation

- Despite being theoretically unbiased, CV can still overfit
- A multistage validation approach protects against this
- CV also invalidates parametric tests (more later)







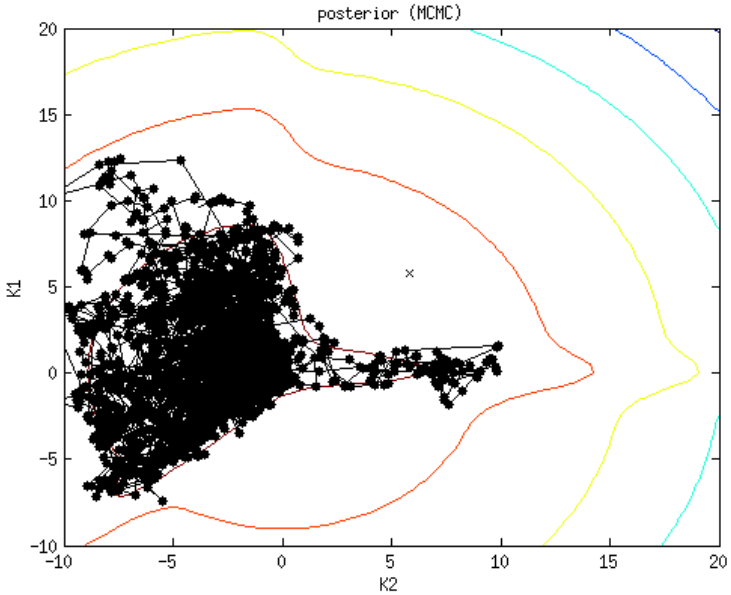
Varoquaux et al. (2017)

Bayesian parameter optimisation

- Bayesian models also depend on multiple variance/noise hyperparameters

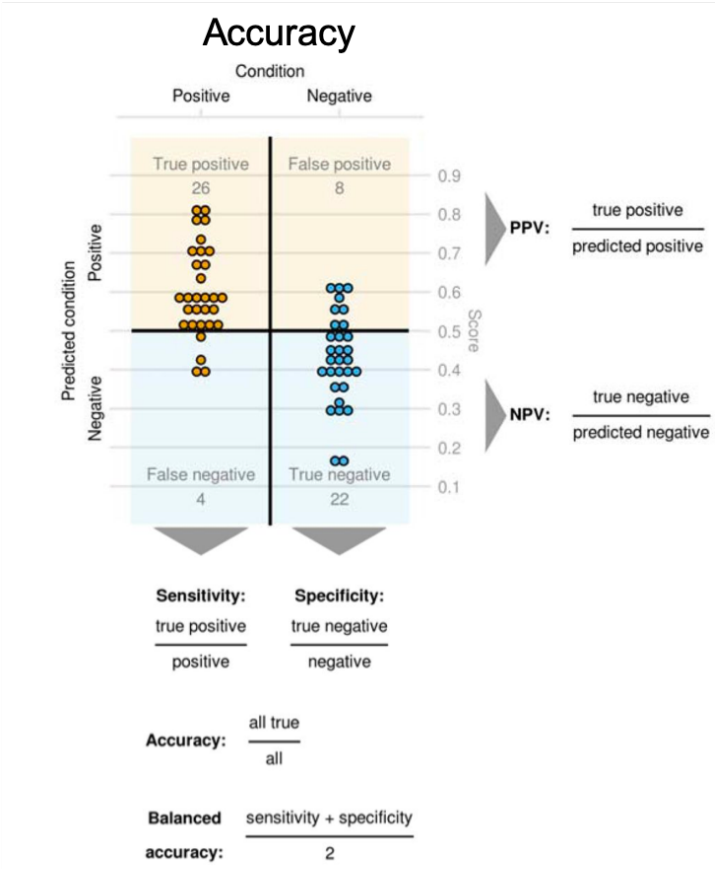
$$p(\boldsymbol{w}|\boldsymbol{y},\theta,\sigma) = \frac{p(\boldsymbol{y}|\boldsymbol{w},\sigma)p(\boldsymbol{w}|\theta)}{p(\boldsymbol{y}|\theta,\sigma)}, \quad p(\boldsymbol{y}|\theta,\sigma) = \int p(\boldsymbol{y}|\boldsymbol{w},\sigma)p(\boldsymbol{w}|\theta)d\boldsymbol{w}$$

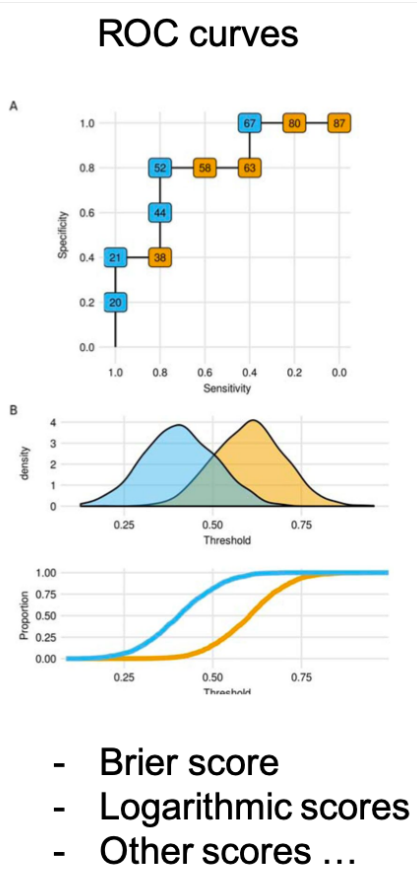
- Many approaches: nested CV, Empirical Bayes, MCMC ...



Statistical assessment of model performance

1. Choice of error measure





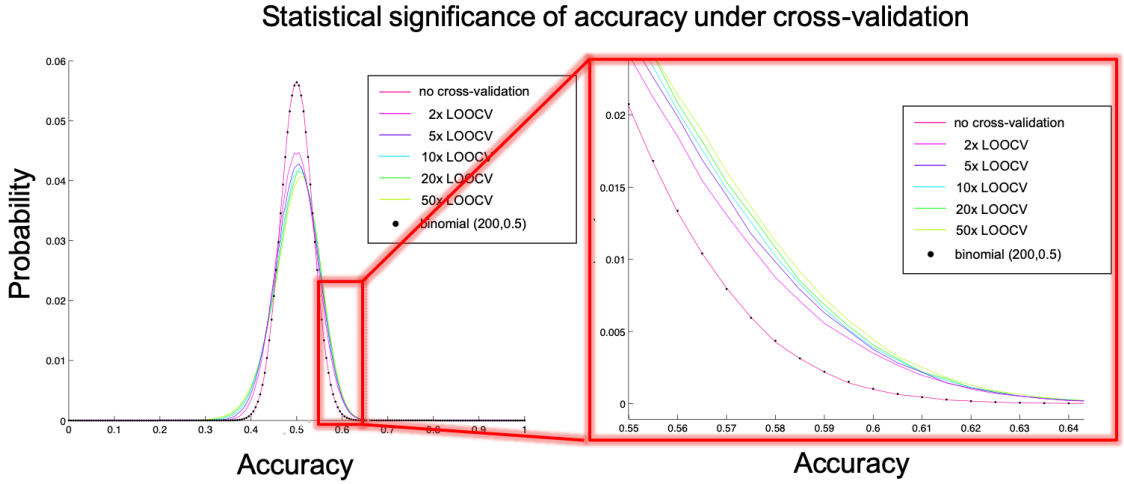
- Brier score
- Logarithmic scores
- Other scores ...

- Also many regression measures (explained variance, MSE,...)
- DIfferent error metrics are sensitive to different aspects (e.g. MSE depends on the scale of the data) *Dinga et al. (2019)*

Choice of error metric

2. Statistical testing framework. There are various options:
   - Parametric tests (e.g. binomial test, t-test)
   - Randomization tests (permutation, bootstrapping)

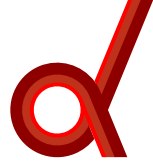
- Cross-validation induces dependency between the folds invalidating parametric statistics



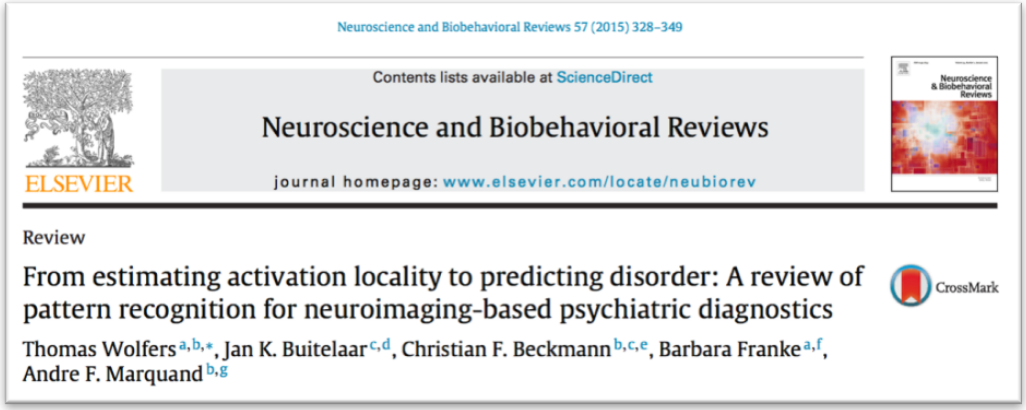
- Parametric assumptions may not be met (e.g. interval data)
- Permutation tests must respect *exchangeability*, e.g. site effects, family structure ...

Stelzer et al. (2013); Winkler et al. (2015)

Outline



Supervised learning for automated diagnosis and prognosis



Neuroscience and Biobehavioral Reviews 57 (2015) 328–349

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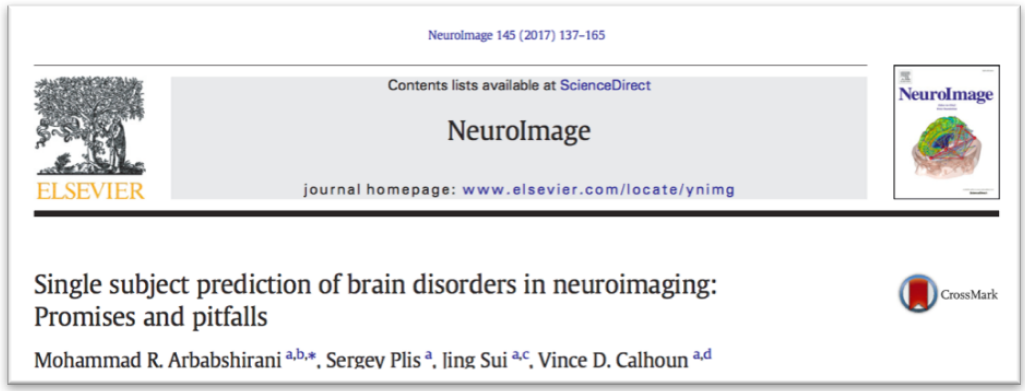
Review

From estimating activation locality to predicting disorder: A review of pattern recognition for neuroimaging-based psychiatric diagnostics

Thomas Wolfers[a,b,*], Jan K. Buitelaar[c,d], Christian F. Beckmann[b,c,e], Barbara Franke[a,f], Andre F. Marquand[b,g]



NeuroImage 145 (2017) 137–165

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Single subject prediction of brain disorders in neuroimaging: Promises and pitfalls

Mohammad R. Arbabshirani[a,b,*], Sergey Plis[a], Jing Sui[a,c], Vince D. Calhoun[a,d]

nature neuroscience

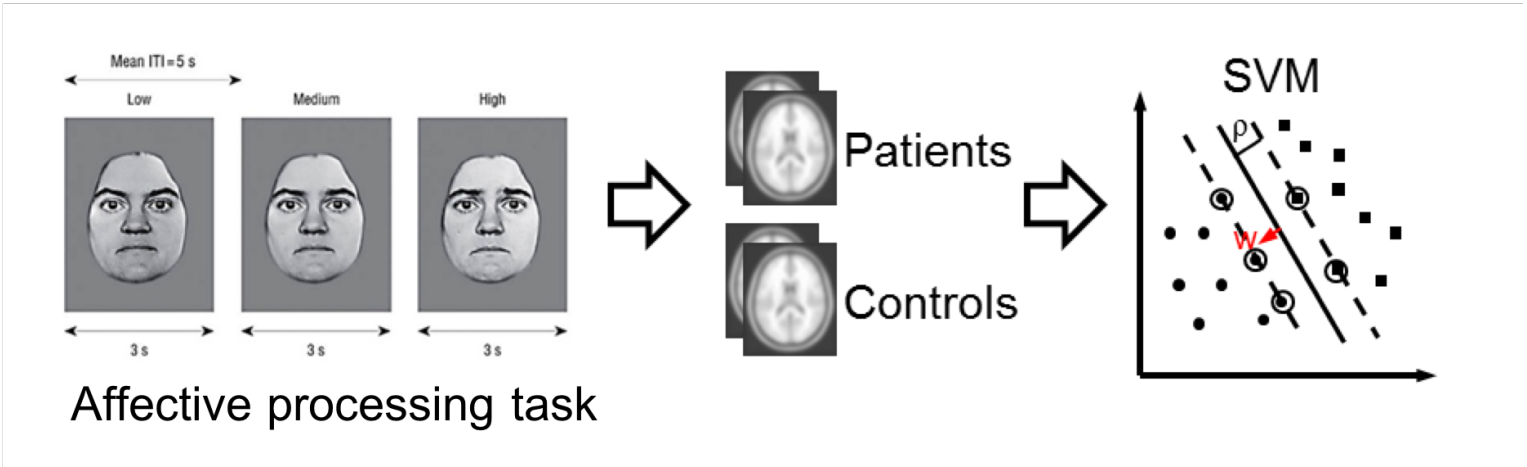
Building better biomarkers: brain models in translational neuroimaging

Choong-Wan Woo[1–4], Luke J Chang[5], Martin A Lindquist[6] & Tor D Wager[3,4]

Wolfers et al. (2015); Arbabshirani et al. (2017); Woo et al. (2017)

Supervised learning for depression diagnosis

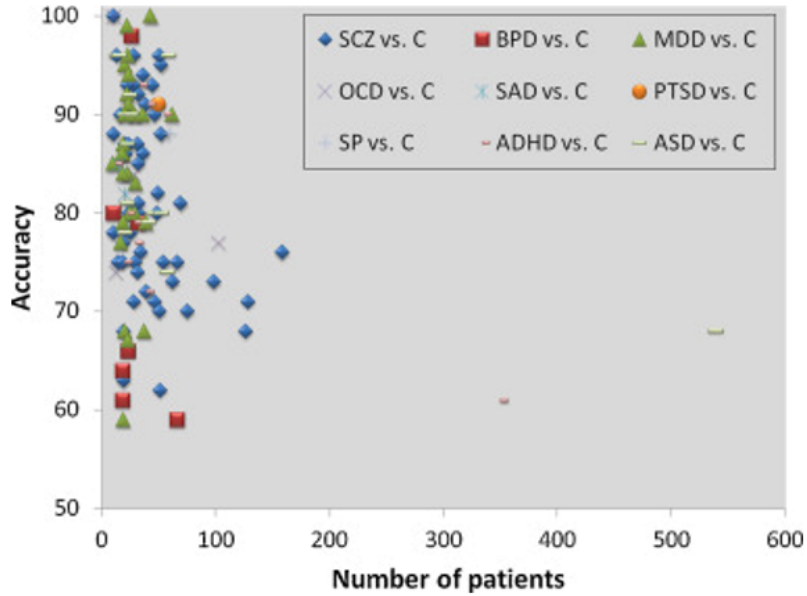
This study was an early application of Pattern recognition to predict disease state in major depression



- Patients could be discriminated from controls with 87% accuracy
- Patients who responded well to fluoxetine could be discriminated from non-responders with 67% accuracy

Fu et al. (2008)

Where are we now?

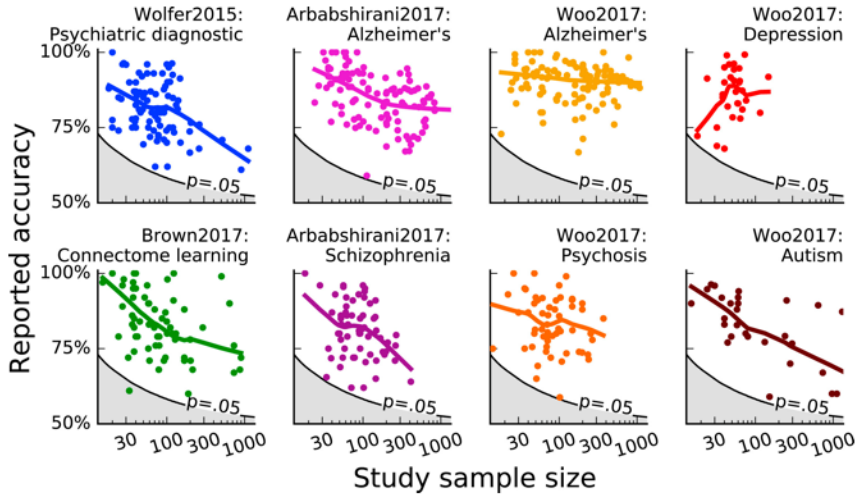


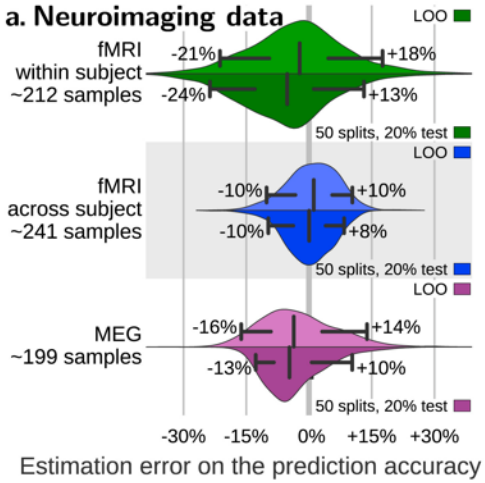
- 116 studies
- Most disorders
- Many data modalities

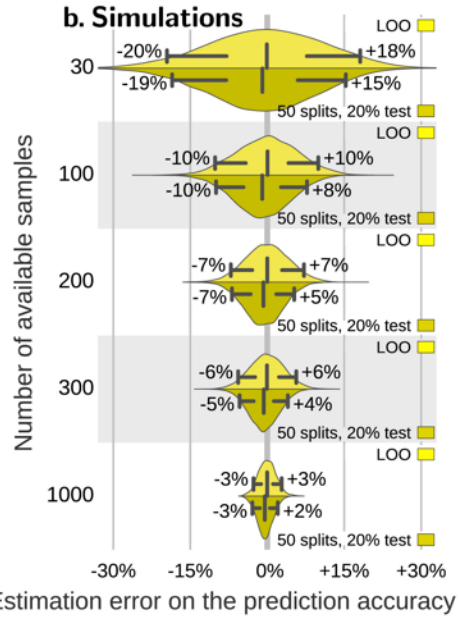
- Moderate acccuracy, highly variable across studies
- Mostly small samples, minimal validation across cohorts
- Accuracy in small samples is extremely variable
- **Heterogeneity** is a major challenge in clinical cohorts

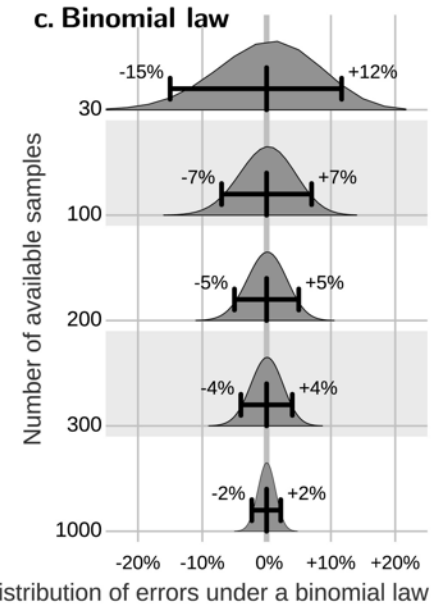
Wolfers et al. (2015)

Cross-validation with small samples



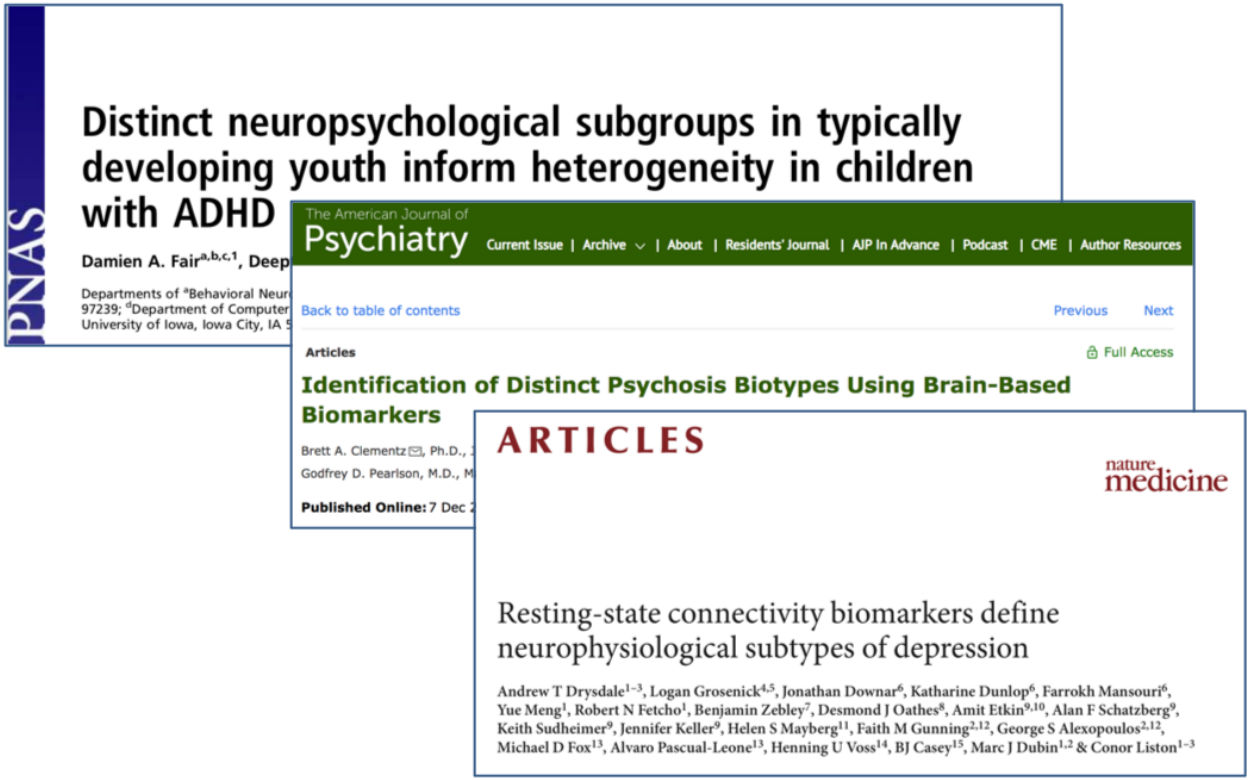






Varoquaux (2017)

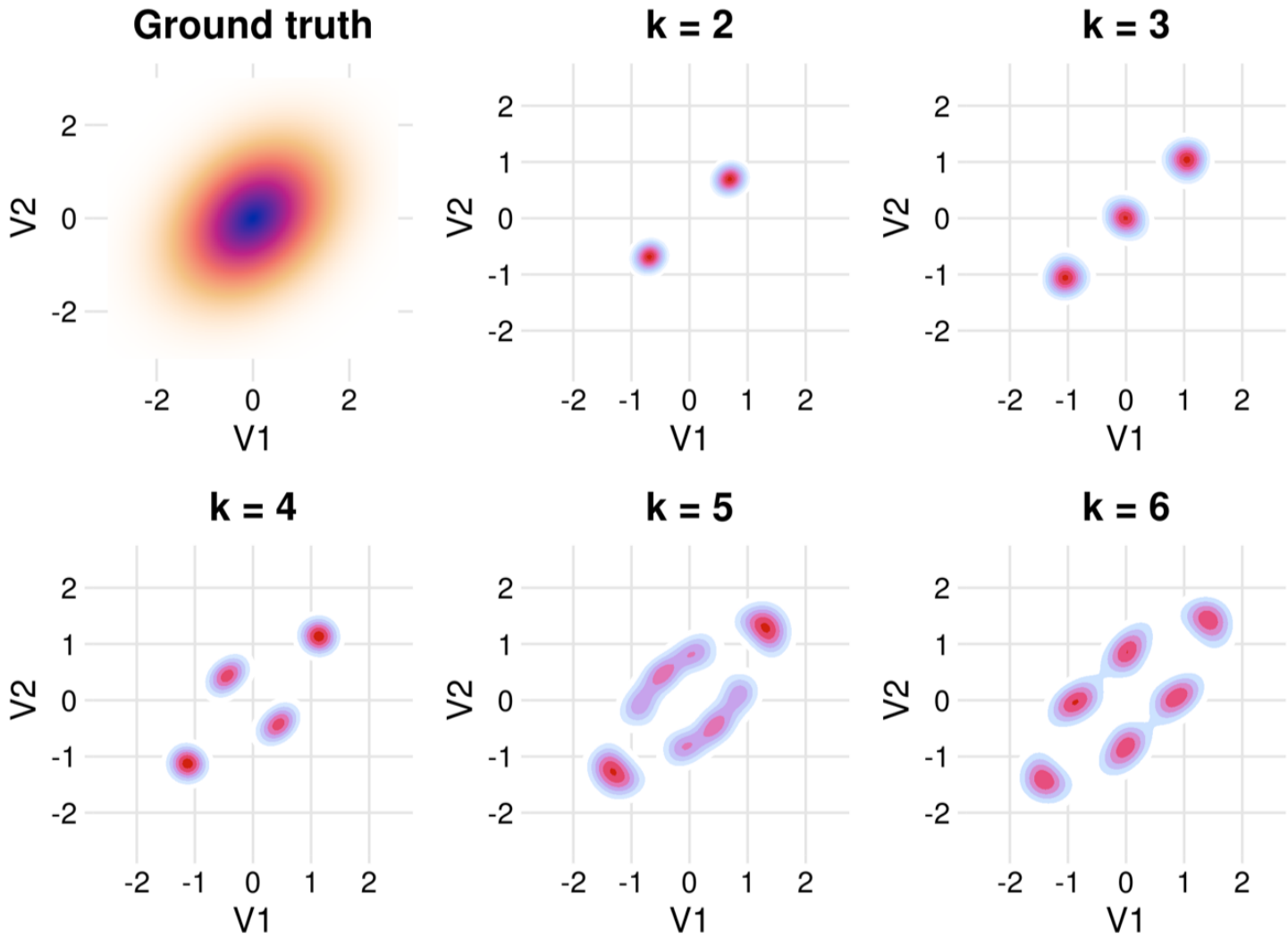
Subtyping psychiatric disorders



Validation of clusters is difficult:

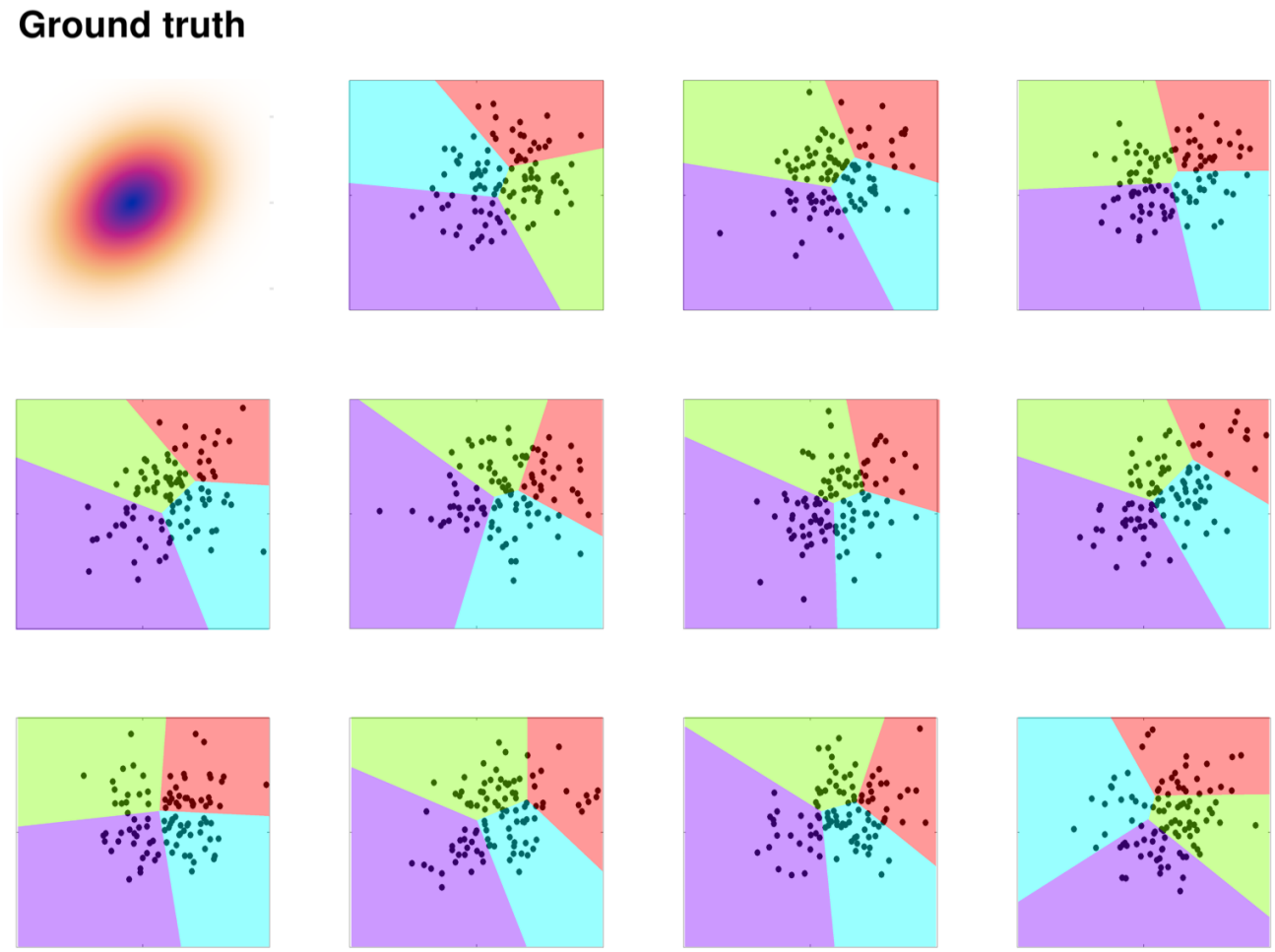
- Clustering always gives a result and there is no clear measure of success (e.g. stability? separability? predictive ability?)
- Rarely test against the 'null' hypothesis that there are no clusters in the data
- Clustering using symptoms may not map onto biology

Issues with clustering



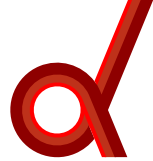
Graphic courtesy of Richard Dinga

Issues with clustering



Graphic courtesy of Richard Dinga

Outline



Interim summary

- PR is a powerful tool to perform single subject inference and detect spatially distributed effects
- Useful in clinical neuroscience for:
  1. Making predictions at the subject level (e.g. prognosis)
  2. Stratifying psychiatric disorders
  3. Estimating mappings between brain and behaviour
- Validation of models is extremely important to ensure generalisability
- More on that in Lecture 2 ...

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