

Machine Learning 2: advanced

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Outline



- 1 Beyond classification and regression
- 2 Alternative learning methods for stratification
- 3 More about deep learning
- 4 Understanding model predictions
- 5 Recommendations

Outline

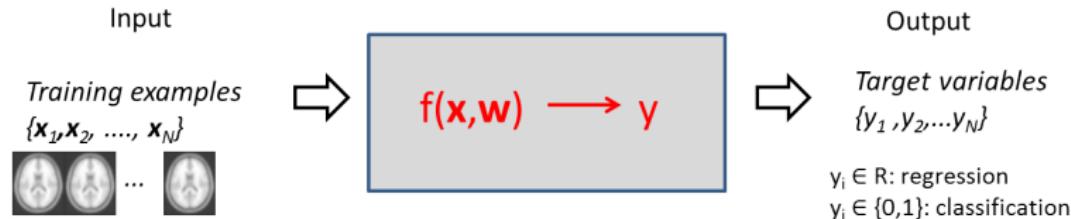


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Types of pattern recognition

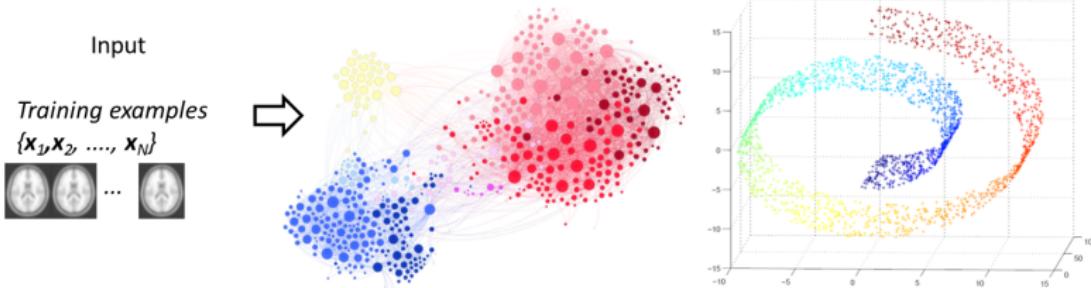


Supervised learning involves learning a mapping between input and output:



In **Unsupervised** learning, algorithms are not provided with output

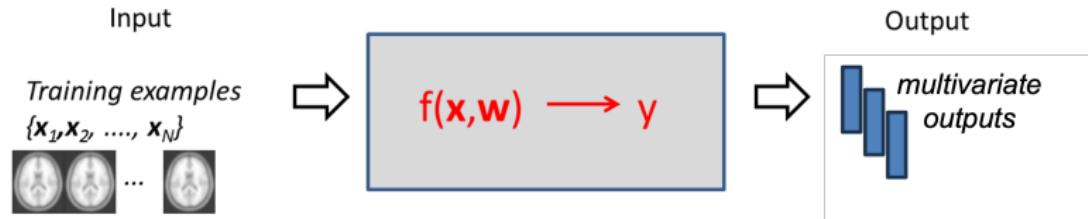
labels and must learn to structure the data by applying heuristics



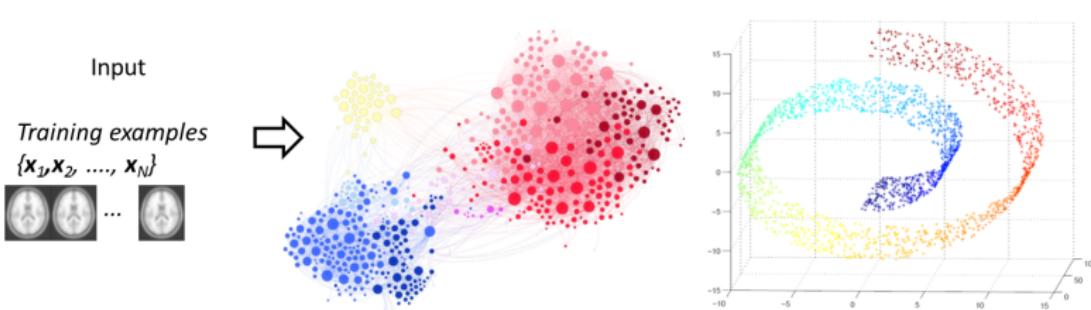
Types of pattern recognition



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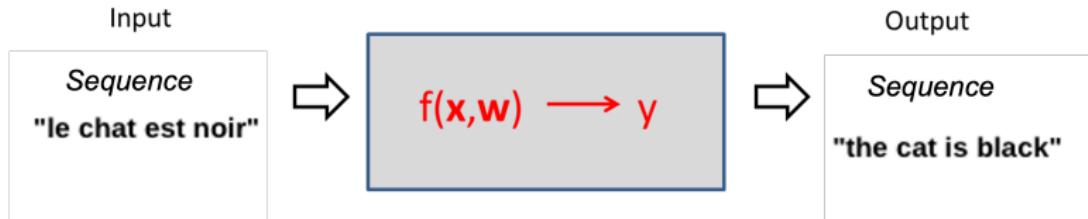
In **Unsupervised** learning, algorithms are not provided with output labels and must learn to structure the data by applying heuristics



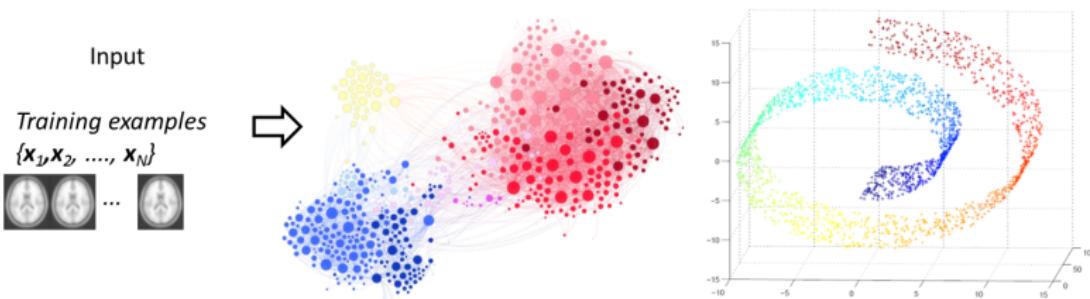
Types of pattern recognition



Supervised learning involves learning a mapping between input and output:



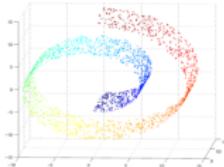
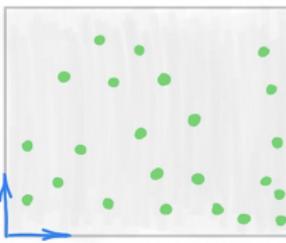
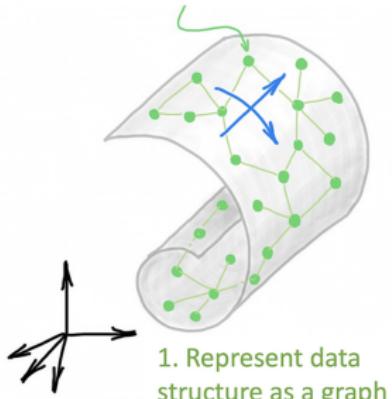
In **Unsupervised** learning, algorithms are not provided with output labels and must learn to structure the data by applying heuristics



Manifold learning



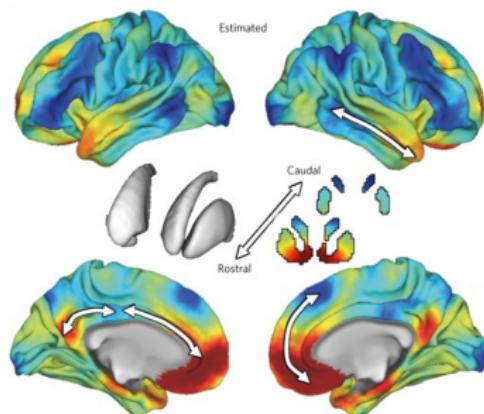
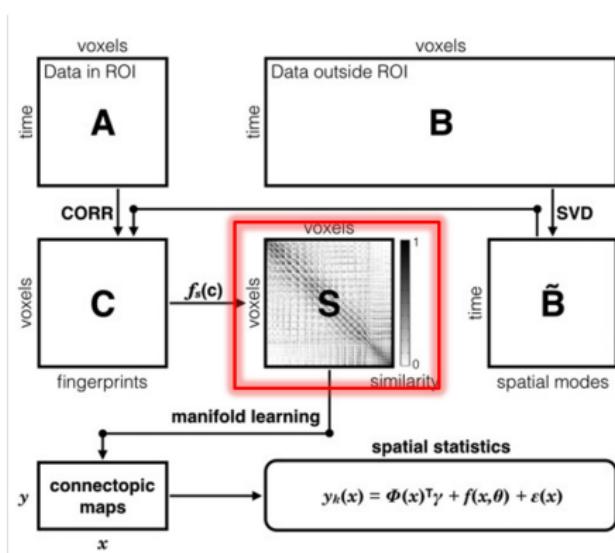
intrinsically low-dimensional
data in a high-dimensional space



- Many different algorithms, diffusion embedding, isomap, Laplacian eigenmaps, autoencoders
- Most use a graph to represent relationships between data points

Image courtesy of Michael Bronstein

Connectopic mapping

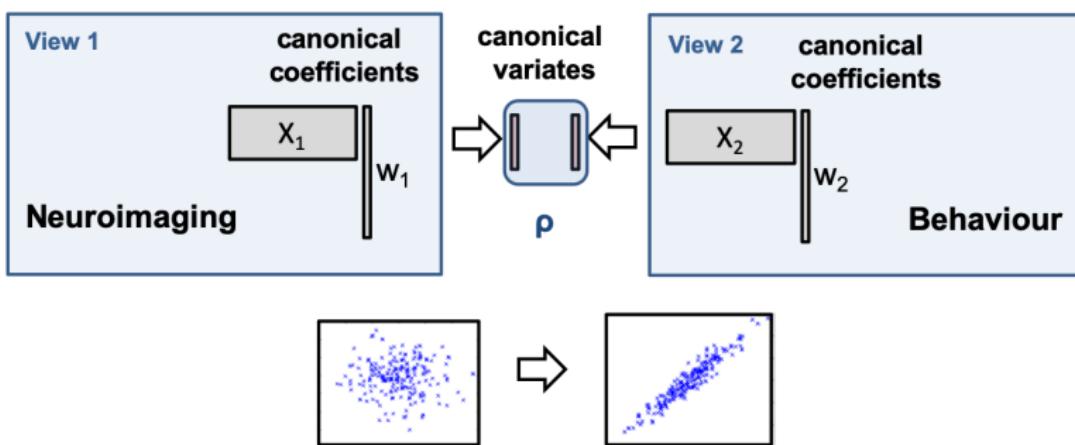


Haak et al. (2016); Marquand et al. (2017)

Learning multivariate mappings



- **Canonical Correlation Analysis** is a standard statistical tool for finding multivariate relationships between datasets
- Generalises Pearson correlation to multiple variables
- Finds projections of the data that maximise the correlation between “views” of the data



Canonical Correlation Analysis



- CCA is related to techniques such as partial least squares
- Formally, CCA solves the following objective function:

$$\max_{w_1, w_2} \text{corr}(X_1 w_1, X_2 w_2)$$

subject to $\|w_1^T X_1^T X_1 w_1\| \leq 1$ and $\|w_2^T X_2^T X_2 w_2\| \leq 1$

where the constraint is sometimes amended to:

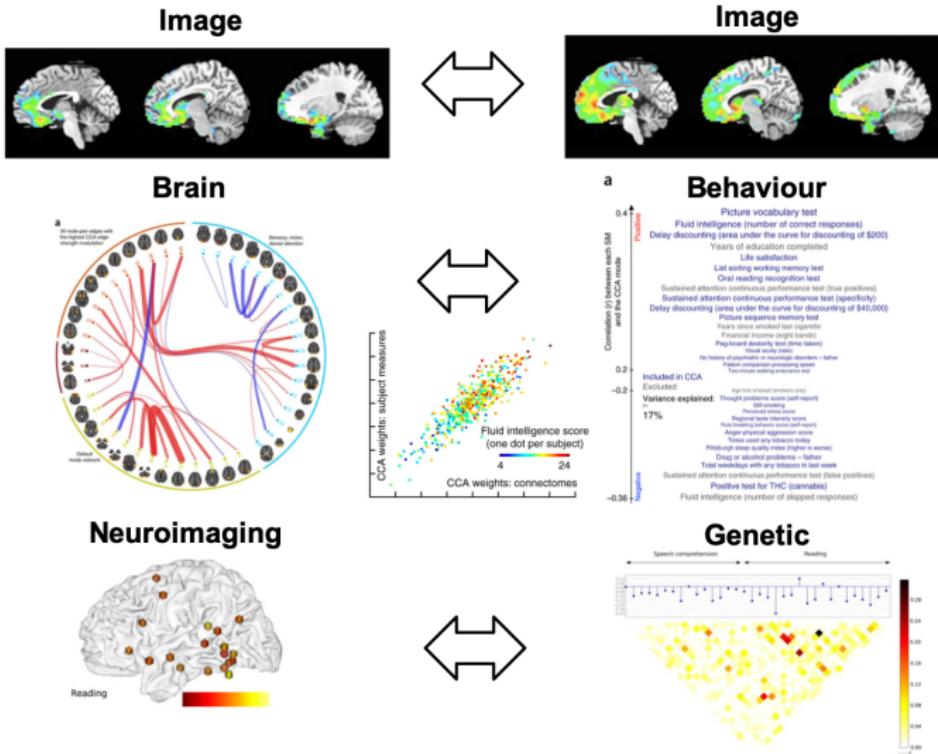
subject to $\|w_1\|^2 \leq 1$ and $\|w_2\|^2 \leq 1$

...and other constraints can be added (e.g. to promote sparsity)

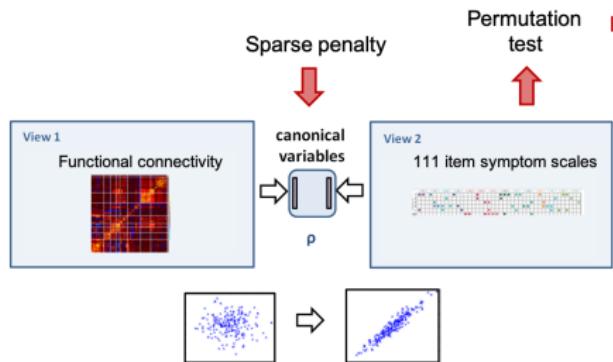
$$P(w_1) < c_1 \text{ and } P(w_2) < c_2$$

- if $n > p_1$ and p_2 , an analytical solution is available
- There are many variants (kernel, Bayesian, deep CCA...)

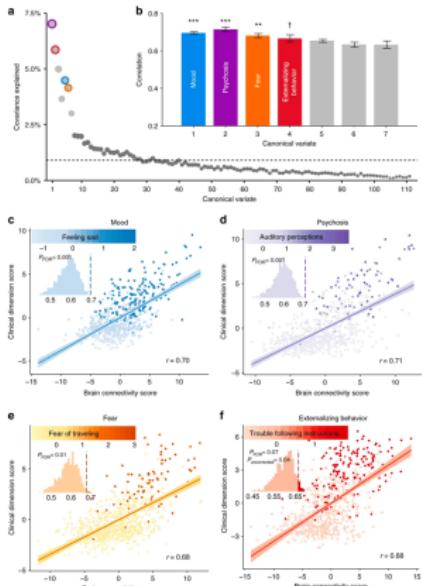
Applications of CCA



Applications of CCA

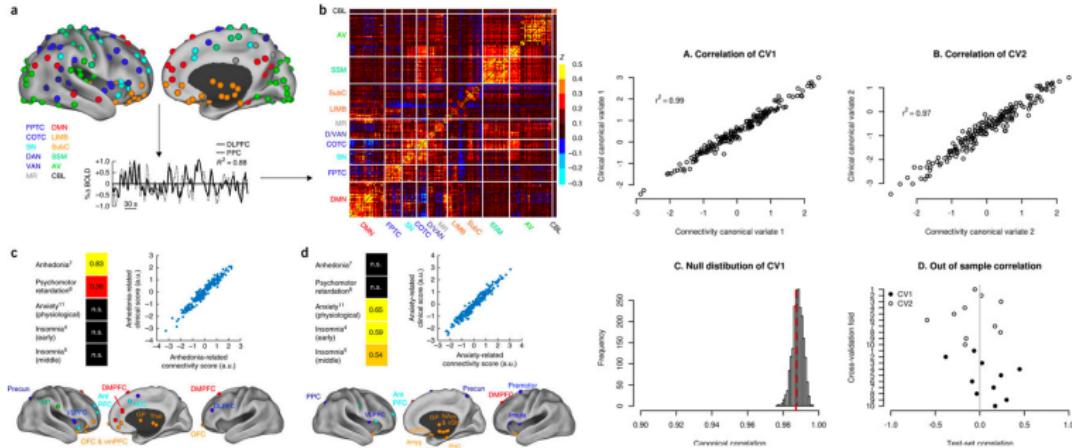


4 Linked dimensions



Xia et al. (2018)

Overfitting in CCA



- CCA easily overfits, even when $N > p$
- In-sample canonical correlation is often high under the null!
- Regularization and/or feature selection is very important
- Statistical evaluation should include the whole pipeline

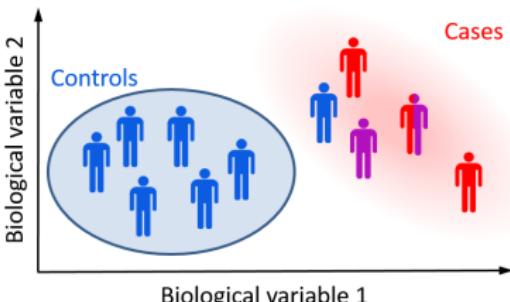
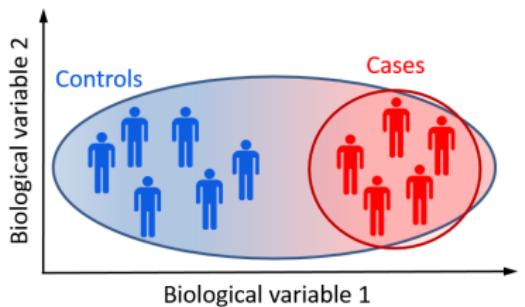
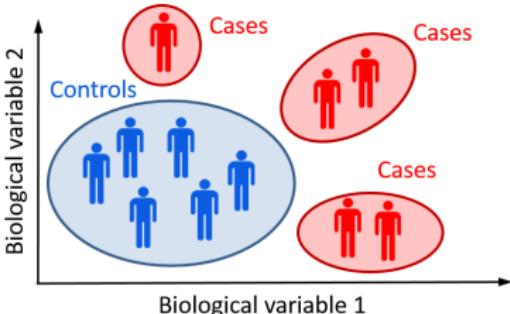
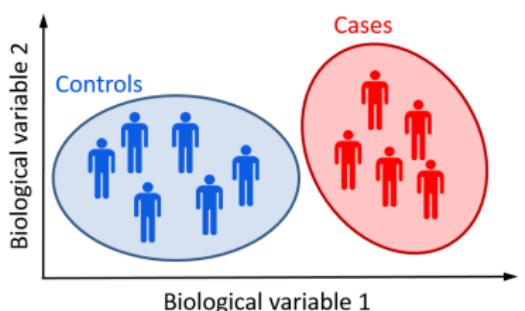
Drysdale et al. (2017); Dinga et al. (2019)

Outline

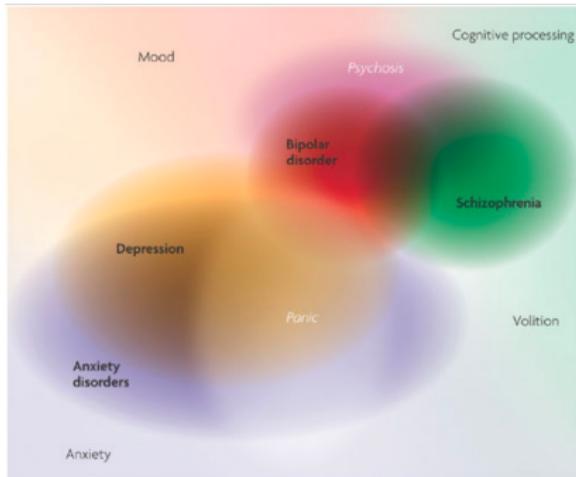


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Many types of heterogeneity



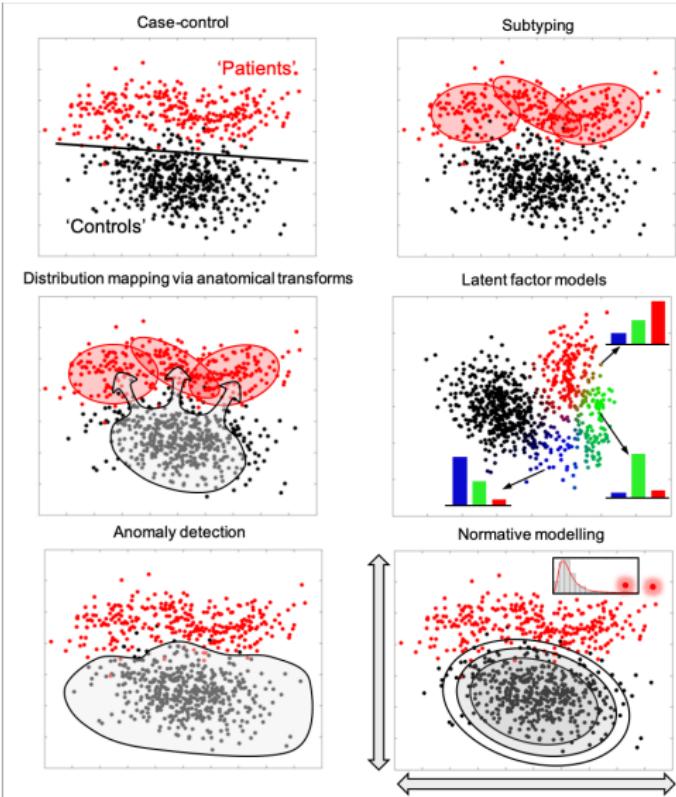
Many types of heterogeneity



Nature Reviews | Genetics

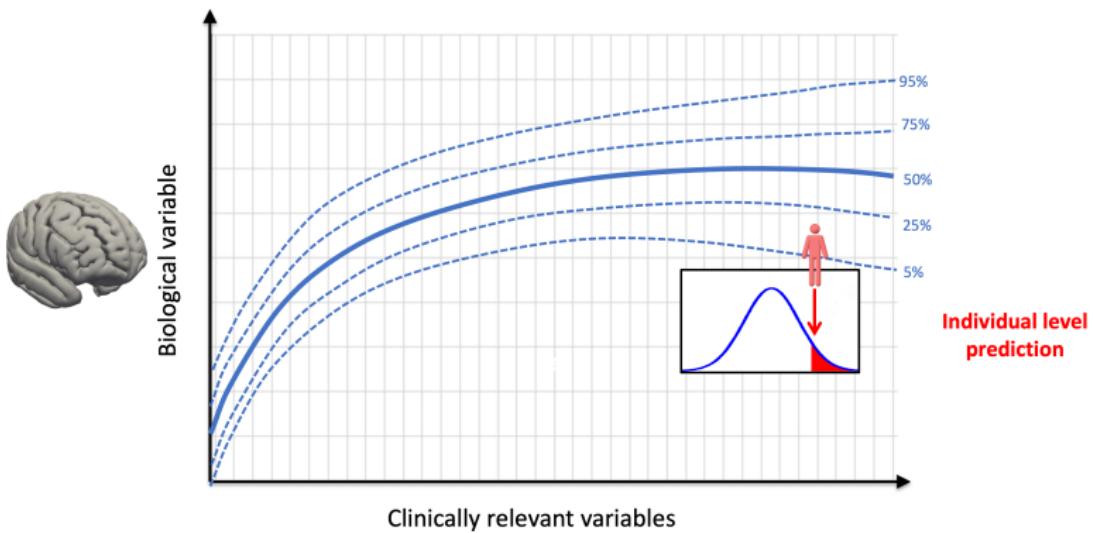
Burmeister et al. (2008)

Methods for addressing heterogeneity



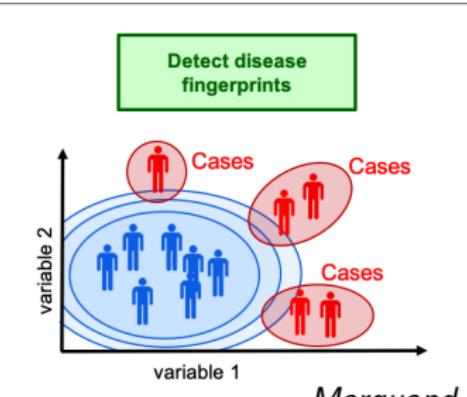
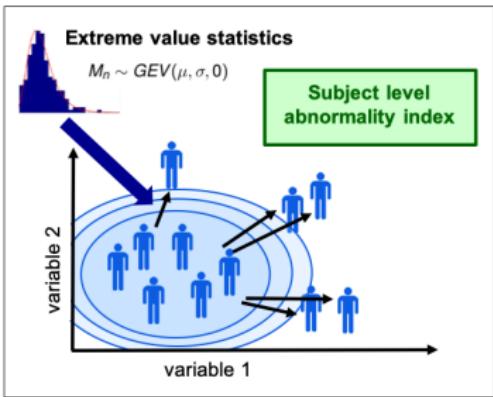
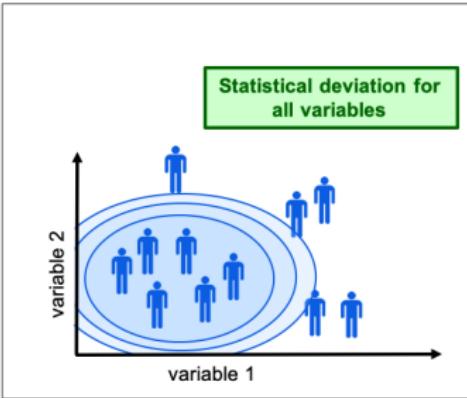
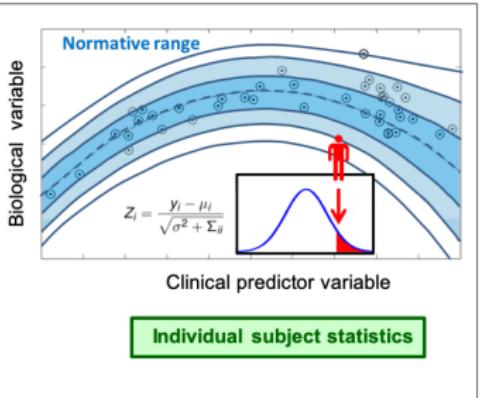
Dong et al. (2016); Zhang et al. (2016); Mourao-Miranda et al. (2011)

Normative modelling



Marquand et al. (2016)

Normative modelling



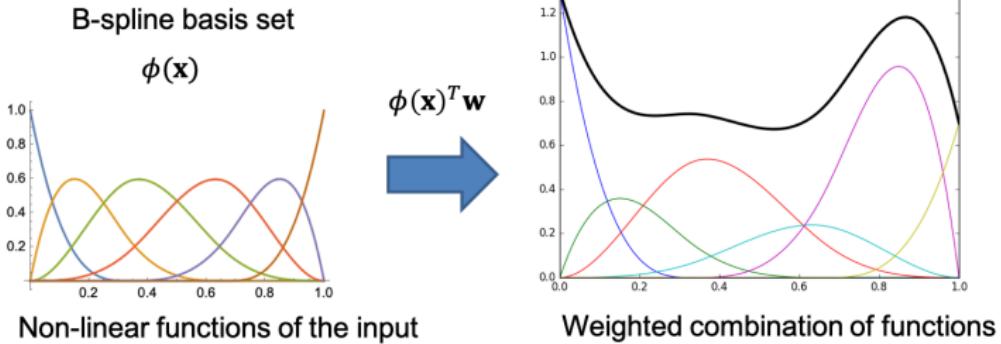
Marquand et al. (2016)

Modelling non-linearity using Bayesian 'linear' regression



- A simple way to model non-linearity is to use a pre-specified basis expansion Φ (e.g. polynomials, RBF, B-spline)

$$p(y|\mathbf{w}, \phi(\mathbf{x}), \sigma) \propto \mathcal{N}(y|\phi(\mathbf{x})^T \mathbf{w}, \sigma) \mathcal{N}(\mathbf{w}|0, \Sigma_{\theta})$$

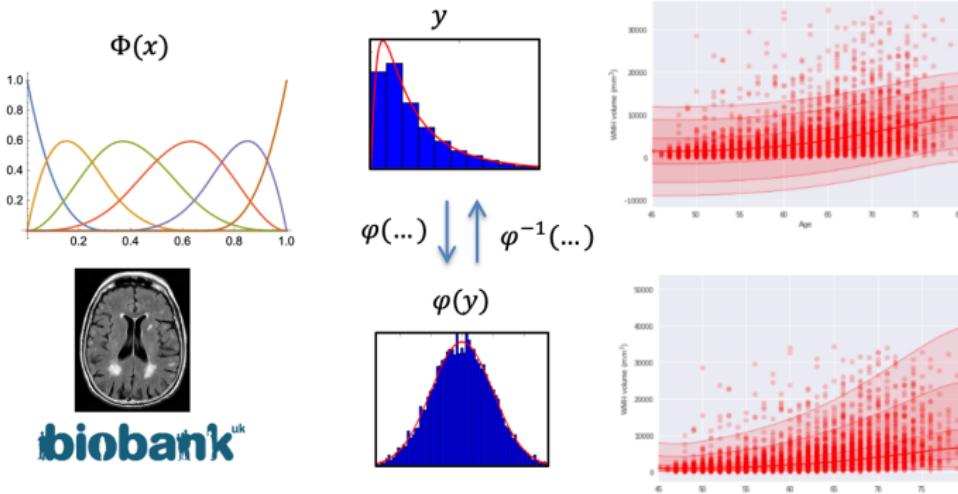


Modelling non-Gaussianity

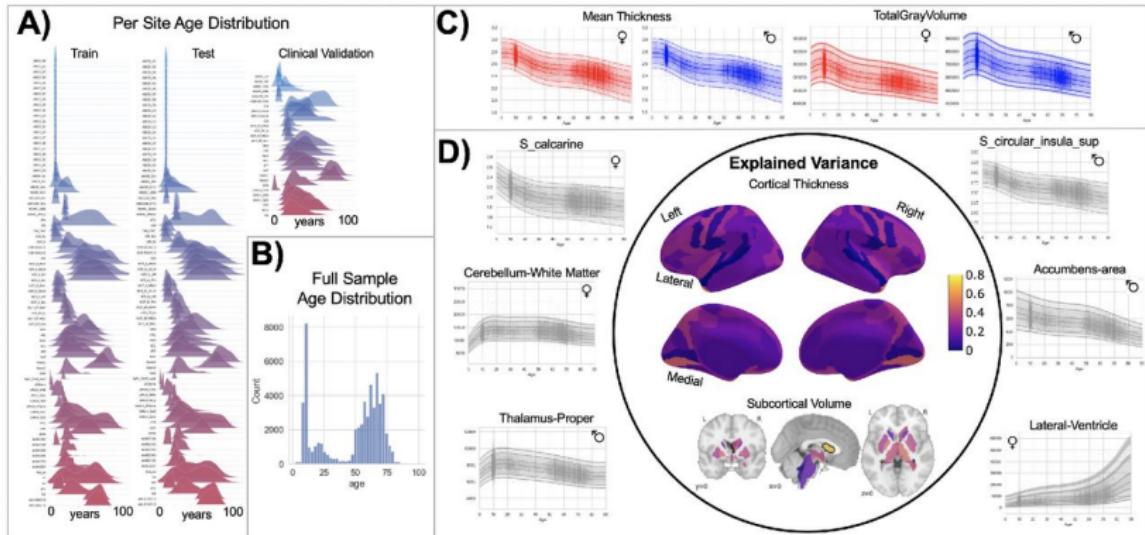


- One way to model non-Gaussian data is to 'warp' the data to a Gaussian space using a non-linear function $\varphi()$

$$p(\varphi(y)|\mathbf{w}, \phi(\mathbf{x}), \sigma) \propto \mathcal{N}(\varphi(y)|\phi(\mathbf{x})^T \mathbf{w}, \sigma) \mathcal{N}(\mathbf{w}|0, \Sigma_\theta)$$



Braincharts across the lifespan



Tutorial: https://github.com/saigerutherford/CPC_MLTutorial

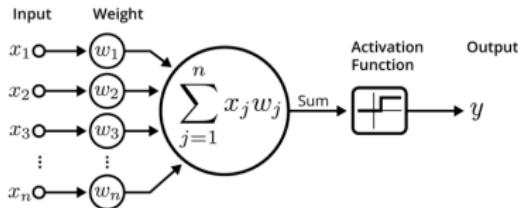
Rutherford et al. (2021a,b)

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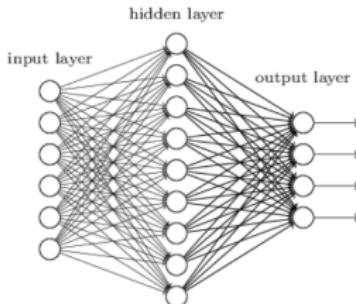


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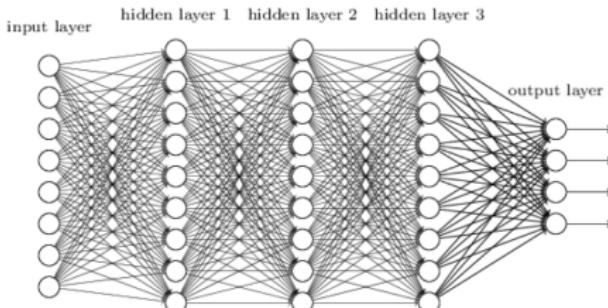
Deep Learning



"Non-deep" feedforward neural network



Deep neural network



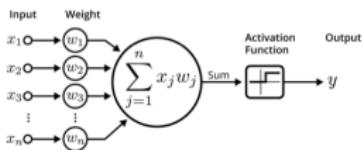
- Many variants but “convolutional” networks are popular
- Predominantly supervised learning
- Usually many parameters to optimise

Deep Learning

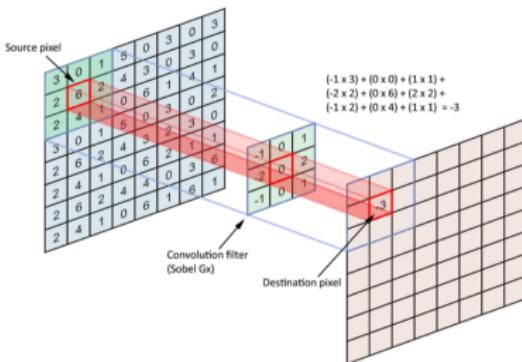
It is helpful to think of deep learning as combining matrix products with point-wise linearity, e.g.:

$$f(x) = \sigma(xW_1 + b_1)W_2$$

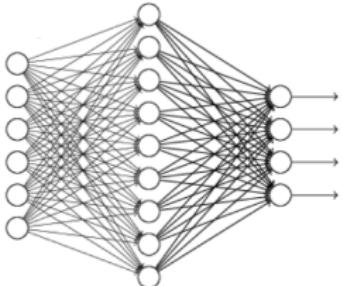
Artificial neuron
(pointwise non-linearity)



Convolution



Fully connected



Max pooling

1	1	2	4
5	6	7	8
3	2	1	0
1	2	3	4

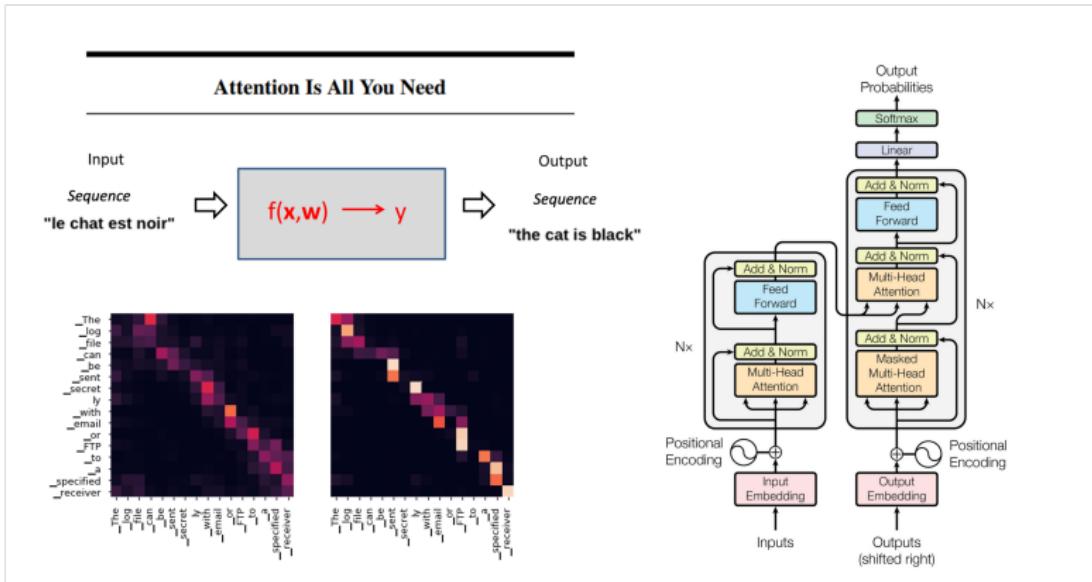
max pool with 2x2 filters
and stride 2

6	8
3	4

Transformers



- Transformers can model long range dependencies in sequence to sequence prediction
 - Uses "attention" to focus on parts of the sequence

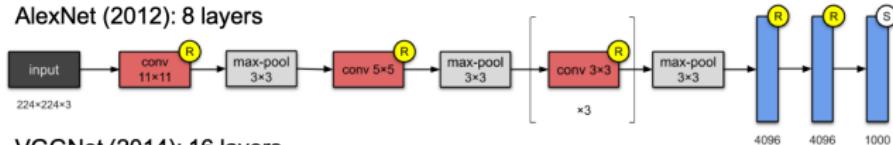


Transformers are at the heart of models like chatGPT

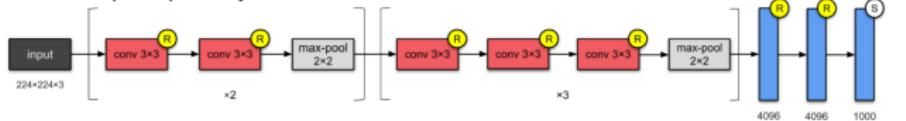
Neural Network Architectures



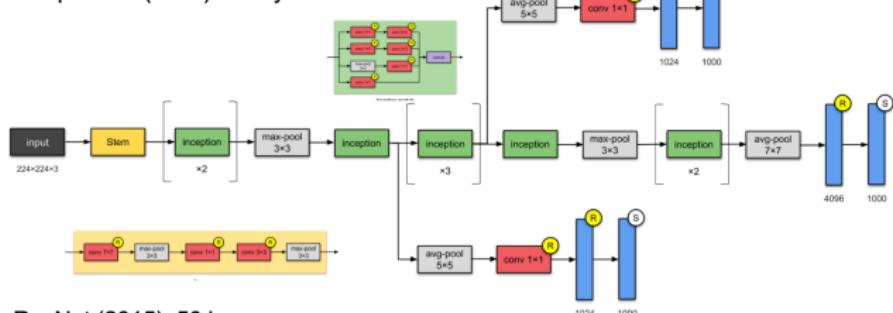
AlexNet (2012): 8 layers



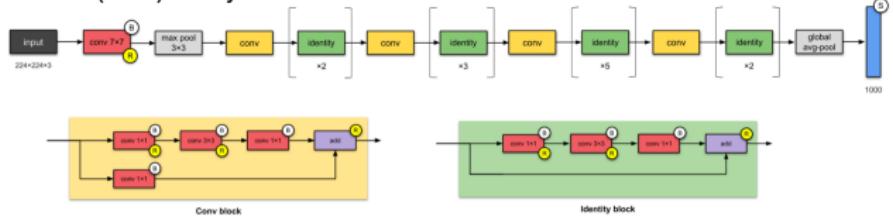
VGGNet (2014): 16 layers



Inception v1 (2015): 22 layers



ResNet (2015): 50 layers





GPT-4 Technical Report

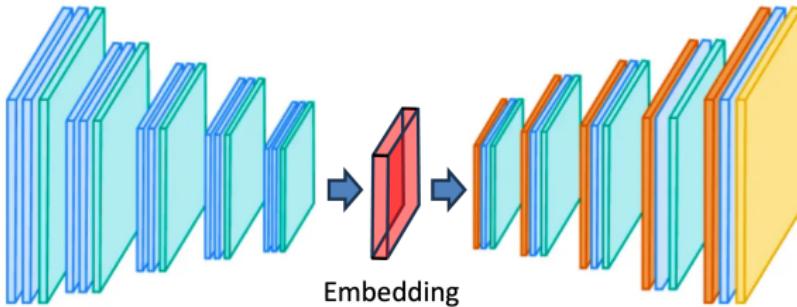
OpenAI*

Given both the competitive landscape and the safety implications of large-scale models like GPT-4, this report contains no further details about the architecture (including model size), hardware, training compute, dataset construction, training method, or similar.

Encoder-Decoder architectures



Encoder



“Le chat is noir”

“A cute kitten riding a skateboard”

Decoder

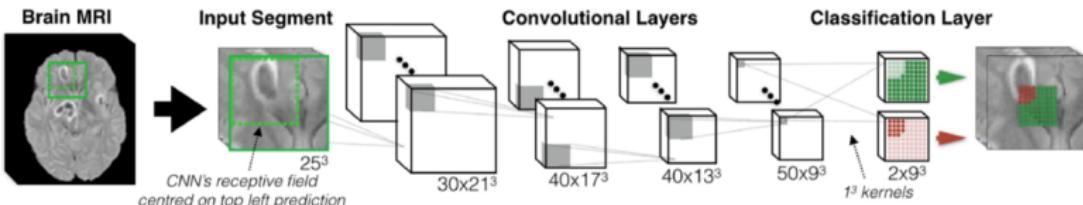
“The cat is black”



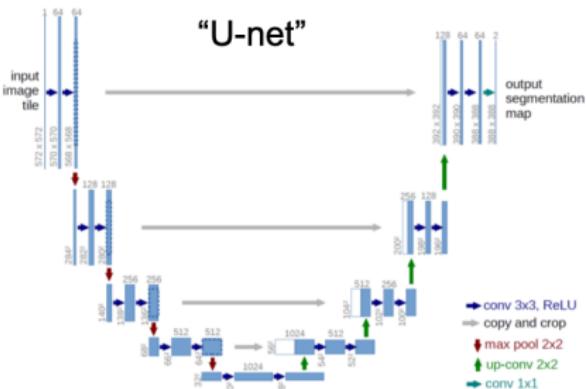
Deep Learning for Segmentation



“DeepMedic”



“U-net”

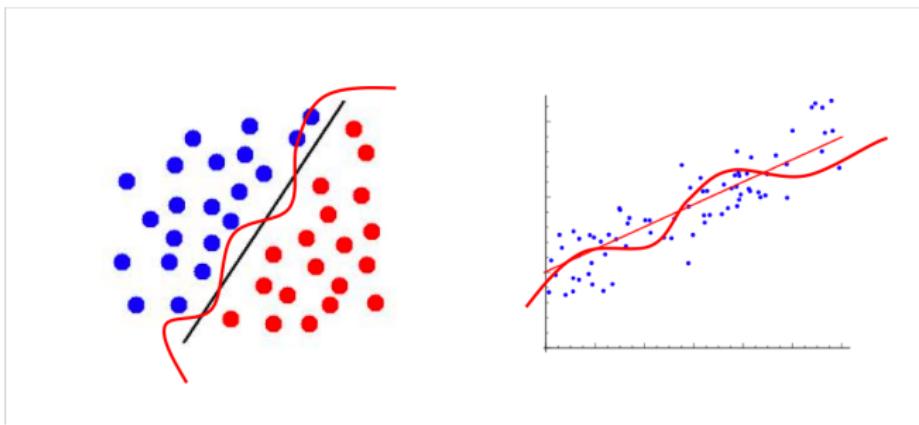


Kamnitsas et al. (2017); Ronneberger et al. (2015)

Overfitting (again)



- But if your problem is linear, your fancy nonlinear algorithm will just overfit

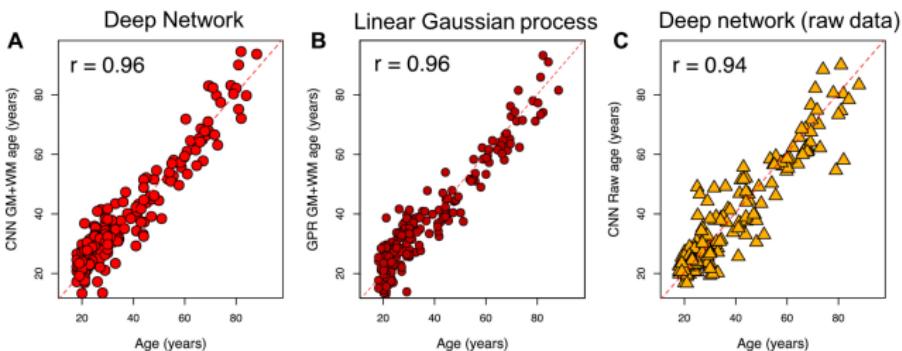
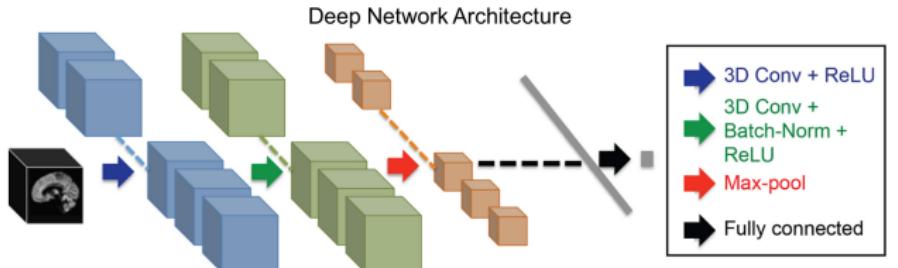


- The more complex the model, the easier it is to overfit
- In complex (deep) models it is often not possible to properly optimise all parameters
- This makes validation extremely important!

Deep Learning in Neuroscience?



- Predict age from $N = 2001$ structural MRI images

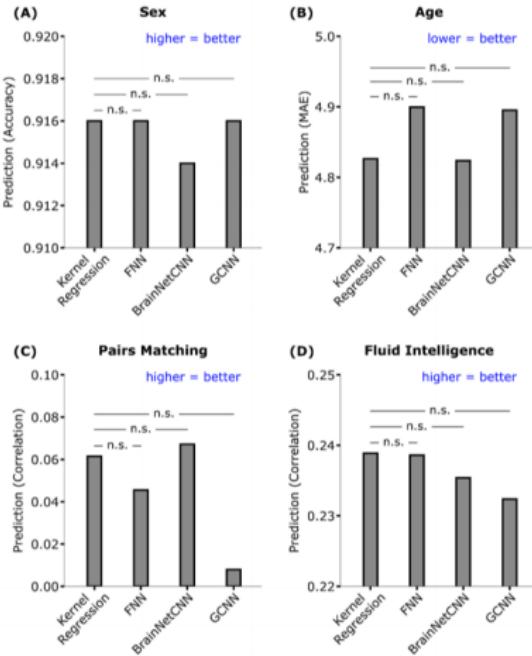


- Similar performance to a linear model on preprocessed data
- Better performance on minimally processed data *Cole et al. (2017)*

Deep Learning in Neuroscience?



biobank^{uk}



Deep Learning in Neuroscience?



New Results

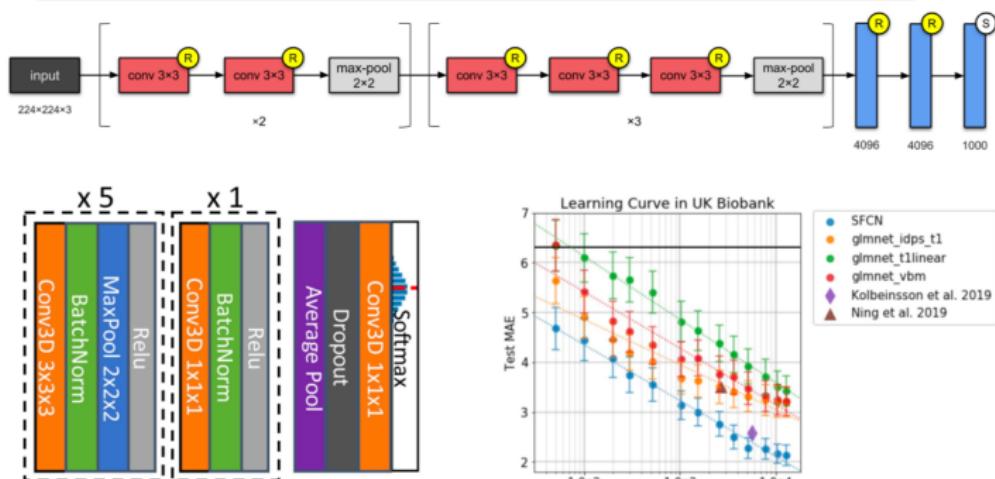
[Comment on this paper](#)

Accurate brain age prediction with lightweight deep neural networks

Han Peng, Weikang Gong, Christian F. Beckmann, Andrea Vedaldi, Stephen M. Smith

doi: <https://doi.org/10.1101/2019.12.17.879346>

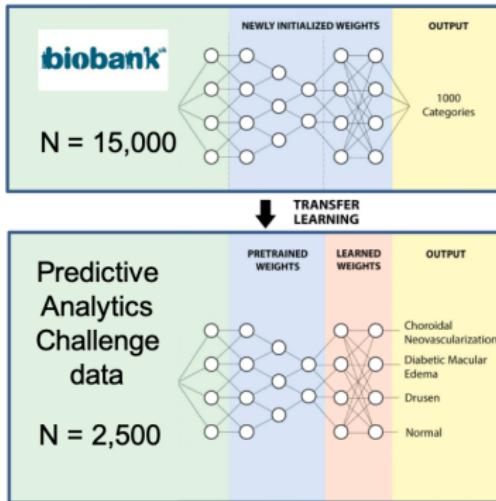
This article is a preprint and has not been certified by peer review [what does this mean?].



Won the 2019 PAC 'brainage' challenge

Peng et al. (2019)

Transfer Learning



- Basic idea: transfer knowledge (i.e. weights) from a large dataset to a small one (where it is harder to learn)
- Different variants depending on whether the targets are the same, similar or different

Deep Learning in Medicine?



- Predict mortality from electronic health records

ARTICLE

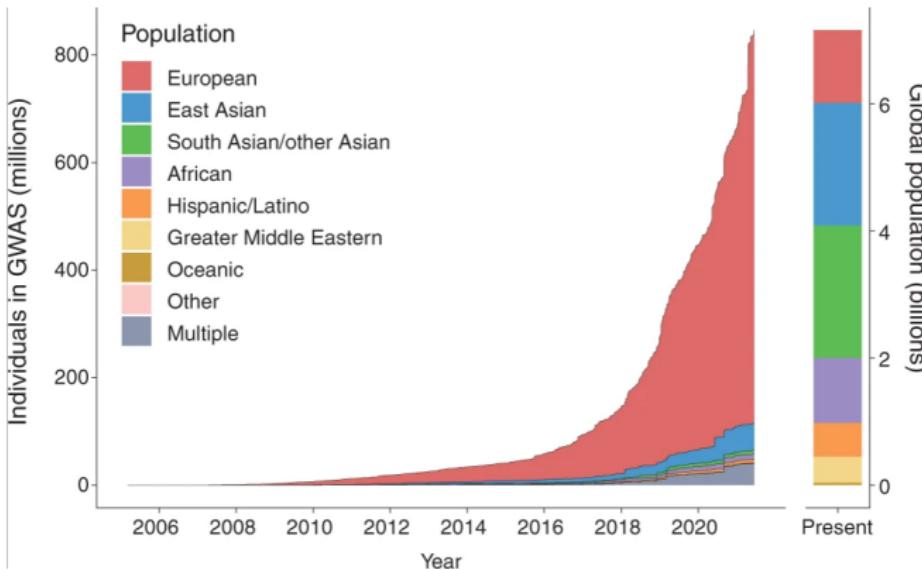
OPEN

Scalable and accurate deep learning with electronic health records

Alvin Rajkomar^{1,2}, Eyal Oren¹, Kai Chen¹, Andrew M. Dai¹, Nissan Hajaj³, Michaela Hardt¹, Peter J. Liu¹, Xiaobing Liu¹, Jake Marcus¹, Mimi Sun¹, Patrik Sundberg¹, Hector Yee¹, Kun Zhang¹, Yi Zhang¹, Gerardo Flores¹, Gavin E. Duggan¹, Jamie Irvine¹, Quoc Le¹, Kurt Litsch¹, Alexander Mossin¹, Justin Tansuwan¹, De Wang¹, James Wexler¹, Jimbo Wilson¹, Dana Ludwig², Samuel L. Volchenboum³, Katherine Chou¹, Michael Pearson¹, Srinivasan Madabushi¹, Nigam H. Shah⁴, Atul J. Butte², Michael D. Howell¹, Claire Cui¹, Greg S. Corrado¹ and Jeffrey Dean¹

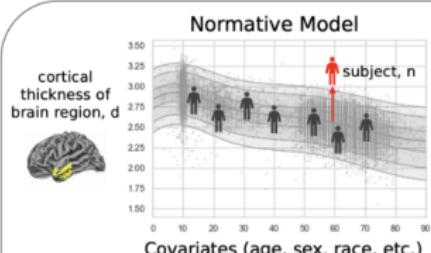
	Hospital A	Hospital B
Inpatient Mortality, AUROC (95% CI)		
Deep learning 24 hours after admission	0.95 (0.94-0.96)	0.93 (0.92-0.94)
Full feature enhanced baseline at 24 hours after admission	0.93(0.92-0.95)	0.91(0.89-0.92)
Full feature simple baseline at 24 hours after admission	0.93(0.91-0.94)	0.90(0.88-0.92)
Baseline (aNEWS ²) at 24 hours after admission	0.85(0.81-0.89)	0.86(0.83-0.88)
30-day Readmission, AUROC (95% CI)		
Deep learning at discharge	0.77 (0.75-0.78)	0.76 (0.75-0.77)
Full feature enhanced baseline at discharge	0.75(0.73-0.76)	0.75(0.74-0.76)
Full feature simple baseline at discharge	0.74(0.73-0.76)	0.73(0.72-0.74)
Baseline (mHOSPITAL ³) at discharge	0.70(0.68-0.72)	0.68(0.67-0.69)
Length of Stay at least 7 days AUROC (95% CI)		
Deep learning 24 hours after admission	0.86 (0.86-0.87)	0.85 (0.85-0.86)
Full feature enhanced baseline at 24 hours after admission	0.85(0.84-0.85)	0.83(0.83-0.84)
Full feature simple baseline at 24 hours after admission	0.83(0.82-0.84)	0.81(0.80-0.82)
Baseline (mLiu ⁴) at 24 hours after admission	0.76(0.75-0.77)	0.74(0.73-0.75)

Be careful about hidden bias!



- There are many examples in healthcare showing biased predictions for marginalised groups
(e.g. African-Americans having a lower probability of being assigned pain medications)

Be careful about hidden bias!

**A)**

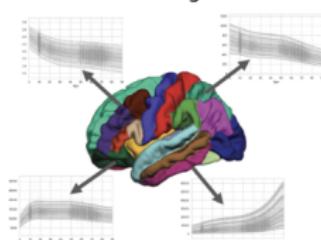
Deviation (Z) score
subject, n
brain region, d

$$z_{nd} = \frac{y_{nd} - \hat{y}_{nd}}{\sqrt{\sigma_d^2 + (\sigma^2)_d}}$$

1. Pre-trained normative models from ~58K people (race unknown)
2. Demographic controlled normative models (**race not included**)
3. Demographic controlled normative models (**race included**)

B)

Fit normative model
for all brain regions

**C)**

Summarize deviation score distributions
(all brain regions) across racial groups



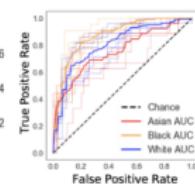
Deviation (Z) Scores

1. Pre-trained
 2. Race not incl.
 3. Race incl.
-

D)

Predict race using deviation scores as features

		True Label	Asian	Black	White
Predicted Label	Asian	0.46	0.13	0.4	
	Black	0.081	0.76	0.16	
White	Asian	0.12	0.15	0.73	
	Black	0.46	0.13	0.4	



Repeat for all 3
normative models
(pre-trained,
race not incl.,
race incl.)



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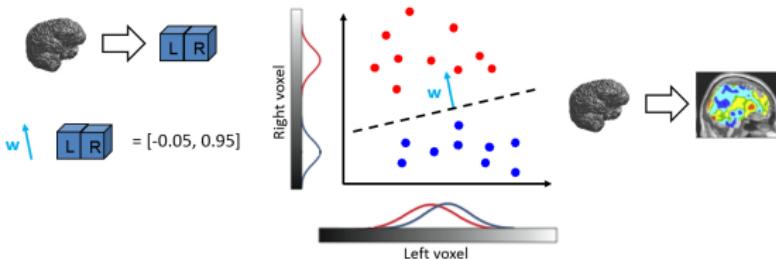
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Mapping the discriminative pattern

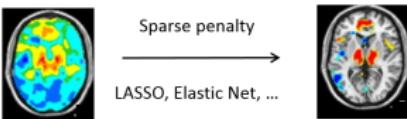


For clinical applications it is crucial to infer which variables drive the predictions. There are multiple options:

- Regional classification accuracy as a proxy (searchlight)
- Explainable AI (relevance propagation, deconvolution, salience, occlusion, ...)
- For linear models, the weights can be directly visualised



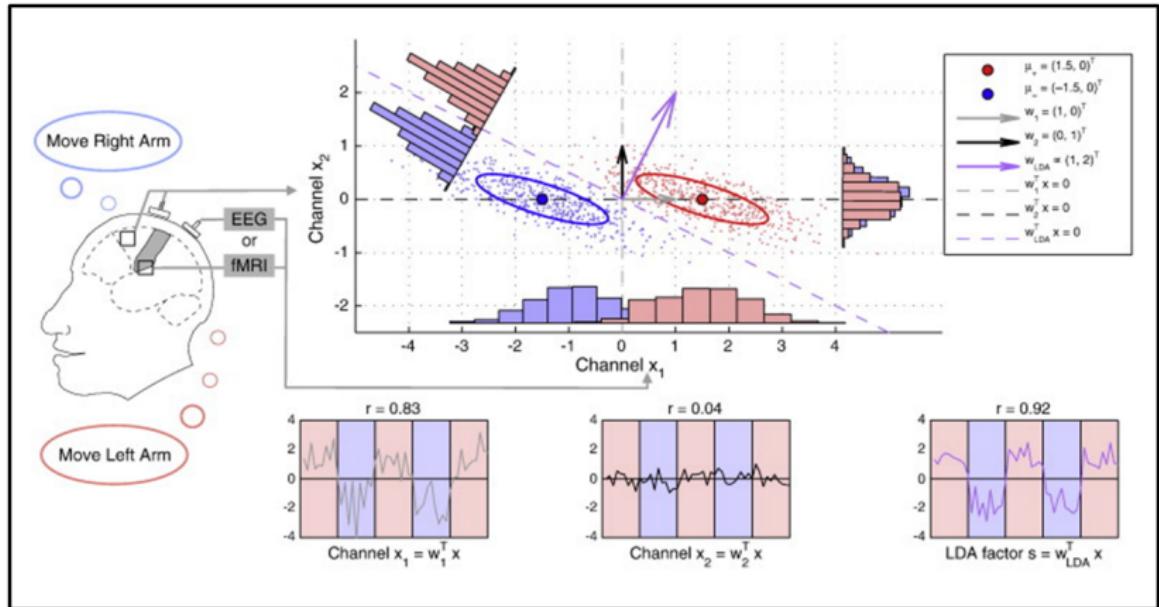
- Can also use regularization to enforce sparsity



- Weights are often regarded as being difficult to interpret, but this is not always true

Weights do not reflect univariate differences

One proposal is to consider the weights from a forward model



Construct 'forward maps' by premultiplying by the data covariance

$$a = \frac{1}{\sigma_y^2} \sum_x w$$

Hauke et al. (2014)

Understanding weights of discriminative models

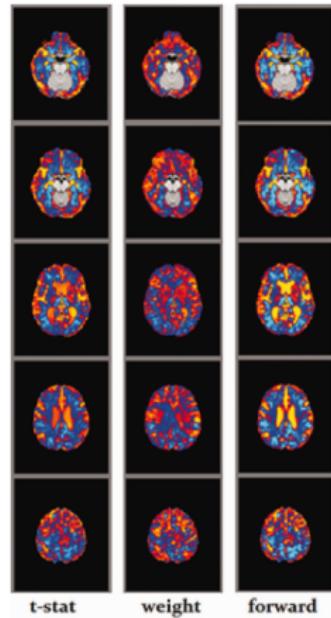
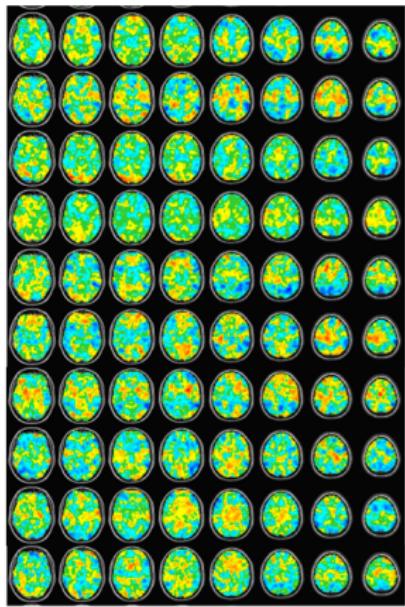


- The correct interpretation of the weights is the contribution of each feature to the predictions. This is the same as in a GLM
- Difficulty arises only due to multicollinearity between predictor variables which inflates the variance of the weights
- A variable can have a high weight because:
 - ① It is associated with the response variable
 - ② It acts as a 'suppressor' variable that helps to cancel out noise or mismatch in other covariates
- To distinguish between these possibilities, we can compute:

$$a \propto \sum_x w = \text{cov}[X, \hat{y}] = \text{corr}[X, \hat{y}]$$

- These are **structure coefficients** from multivariate statistics
- These measure the univariate association between covariate p and the predictions, i.e.: $\rho(x_p, \hat{y})$
- The weights are influenced by collinearity which impact the magnitude and sign of coefficients

Examples of weights



Aksman et al. (2016)

Outline



- 1 Beyond classification and regression
- 2 Alternative learning methods for stratification
- 3 More about deep learning
- 4 Understanding model predictions
- 5 Recommendations



- Machine learning provides powerful tools for single subject inference and detect spatially distributed effects
- Many different approaches beyond simple notions such as 'classification' or 'clustering'

Recommendations

- Linear models are often sufficient: they are fast, interpretable and often perform as well as non-linear methods
- Careful validation is extremely important for all methods to guard against overfitting
- Machine learning can be easily integrated with neurocognitive models (e.g. to assess candidate models)
- Be aware of potential biases! With complex models it is not possible to assess this definititively

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Tutorial on Normative modelling:
https://github.com/saigerutherford/CPC_ML_tutorial

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But what about the penalty?



- Collinearity is well-known in classical GLM settings, where advice is often given to avoid collinearity
- It is true that collinearity impacts on efficiency, but models with collinear predictors are still interpretable
- Collinearity also impacts penalised regression. Recall that:

$$f(x_i, w) = x_i^T w \quad \Rightarrow \hat{w} = \min_w \sum_{i=1}^n \ell(y_i, f_i) + \lambda J(w)$$

- Considering ridge regression, where the objective function is:

$$\hat{w} = \min_w \sum_{i=1}^n \mathcal{N}(w^T x_i, \sigma^2) + \frac{\lambda}{2} \|w\|_2^2$$

- This is equivalent to:

$$\min_w -\frac{1}{2\sigma^2} \left(\sum_{i=1}^n (y_i - x_i^T w)^2 + \lambda w^T w \right)$$

But what about the penalty?



- This is exactly equivalent to finding the MAP estimate of a posterior distribution over w , with prior:

$$\mathcal{N}(0, \sigma^2 / \lambda I)$$

So what does this mean?

- Collinearity influence the magnitude and sign of coefficients
- Including/excluding variables can change both magnitude and sign of coefficients
- When $p > n$, the problem is ill-posed (multiple ways the same prediction can be achieved).
- Regularisation helps to stabilise coefficients, but does not eliminate the problem