Machine Learning for Medical Image Analysis and Imaging Genetics

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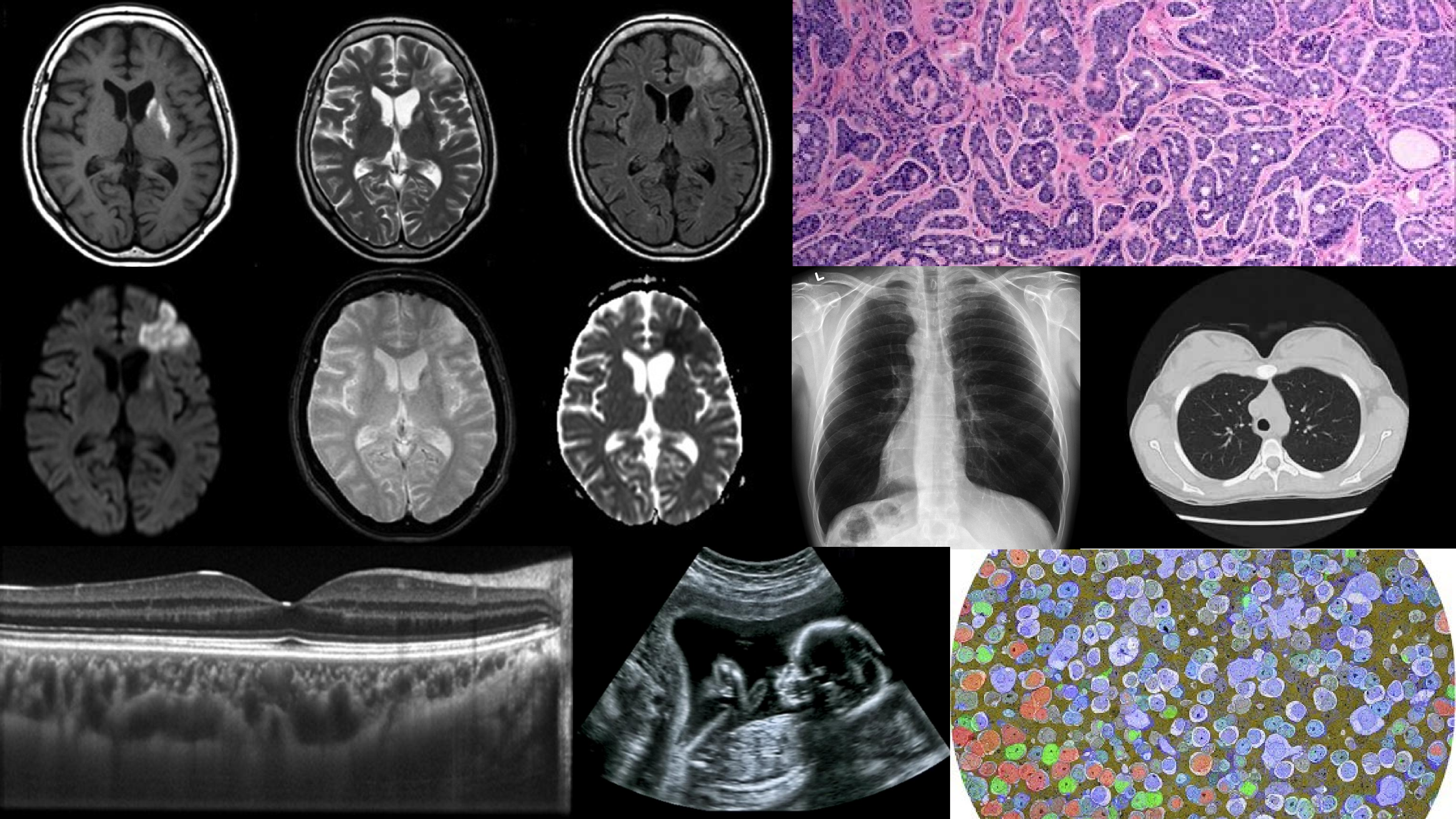
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Outline

- Overview of Medical Imaging
  - Utility and properties
- **Example**: Segmentation
  - *Classical* and deep learning approaches
- **Example**: Registration (alignment):
  - Optimization and learning approaches
- **Example**: Imaging genetics
- Takeaways

Takeaway Goals

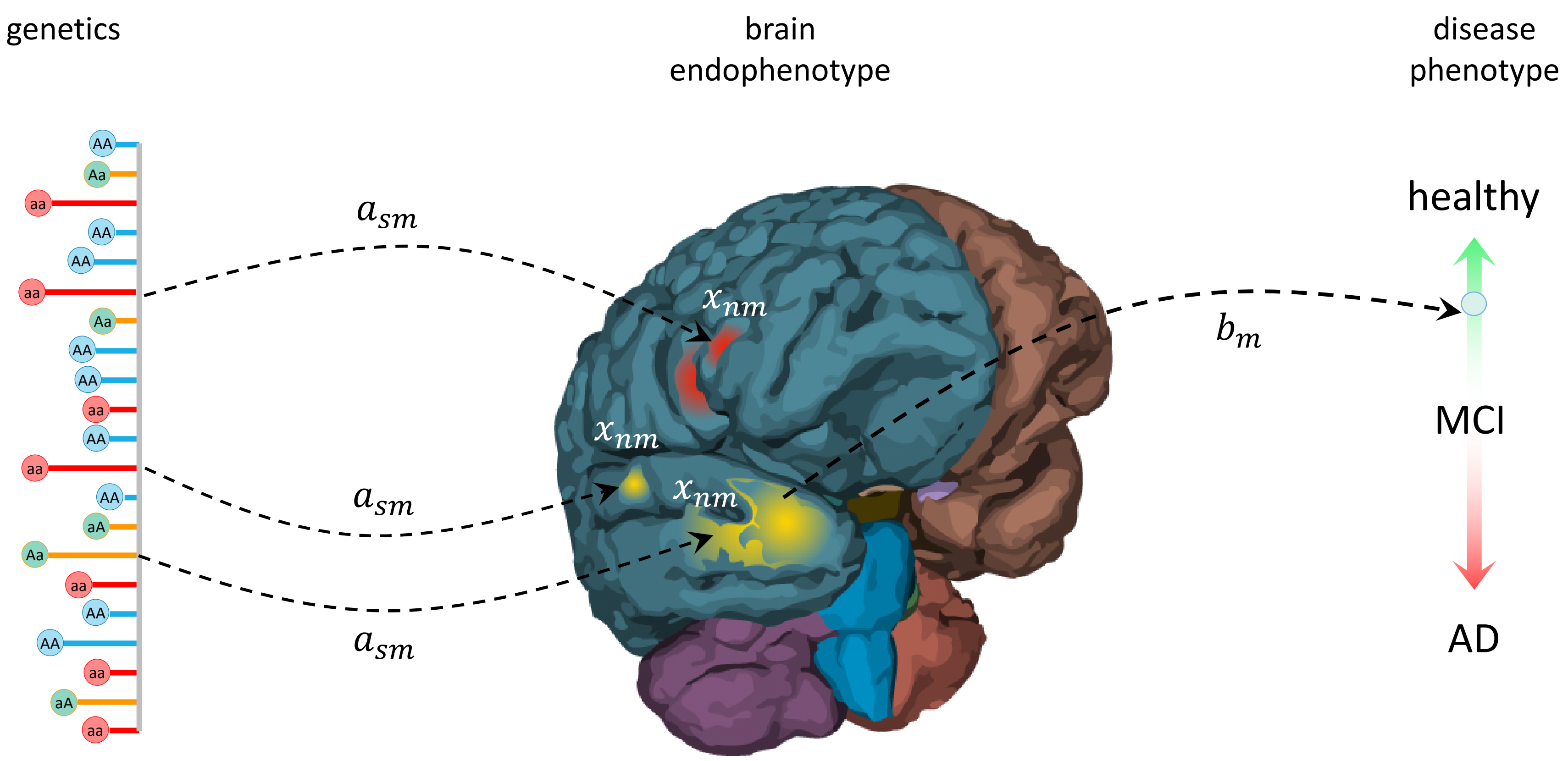
- Problems
  - Help the clinicians or scientists (don’t replace them)
- Tools and approaches
  - Probabilities, convolutions, and anatomical models
  - Clinical interpretation
  - Genetic correlation
- Challenges
  - The systems don’t really work (yet)
- Opportunity
  - Impact healthcare and research!

Medical Imaging

- Crucial tool in clinical practice
  - Diagnostic (and incidental findings)
  - Planning treatment
  - Guide small and large interventions
  - …

Medical Imaging

- Crucial tool in clinical practice
  - Diagnostic (and incidental findings)
  - Planning treatment
  - Guide small and large interventions
  - …
- Research
  - Clinical studies
  - Scientific studies


genetics
brain endophenotype
disease phenotype
AA
Aa
aa
aA
a_{sm}
x_{nm}
b_m
healthy
MCI
AD

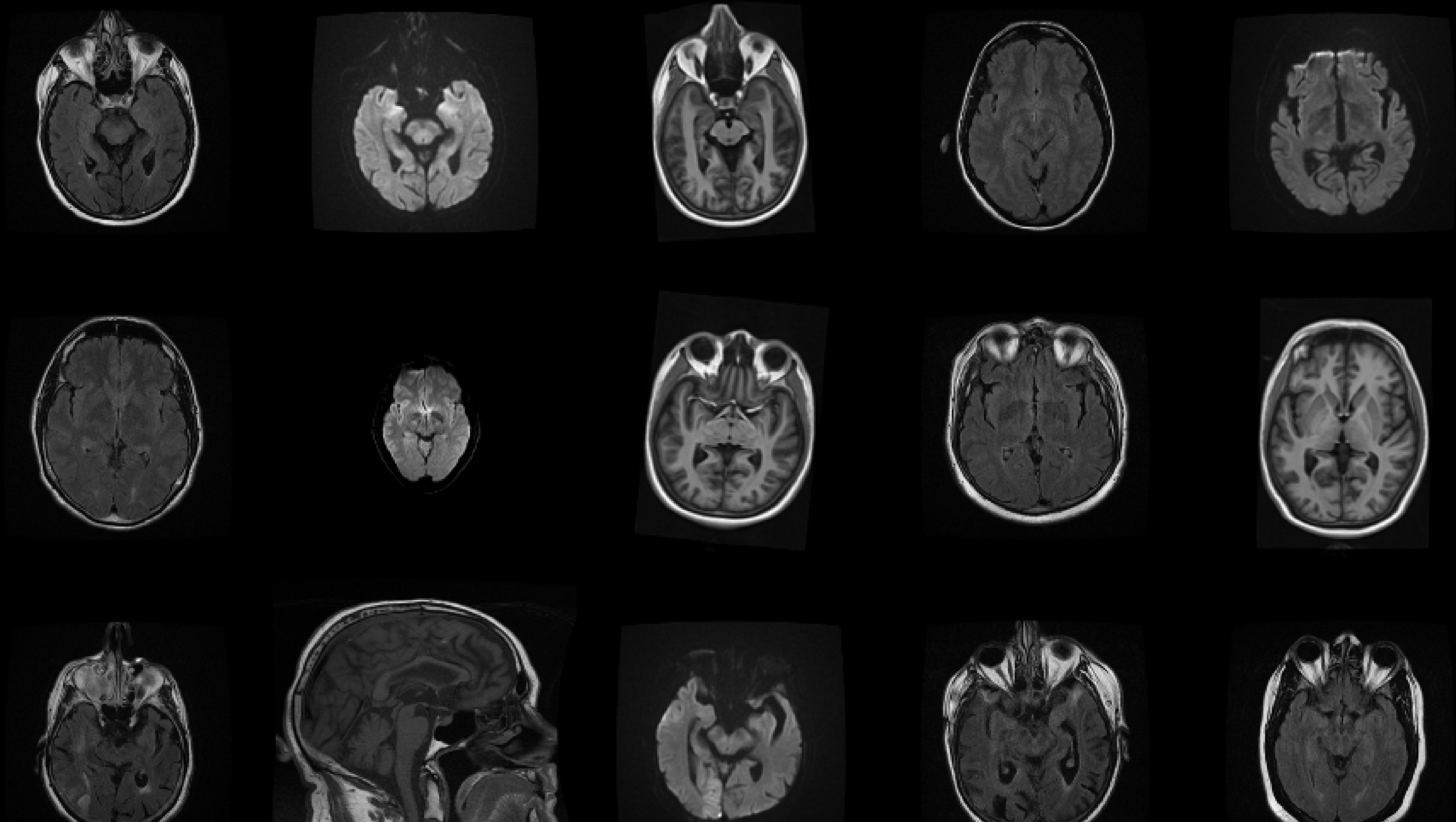
Medical Image **Analysis** (or: how can we help?)

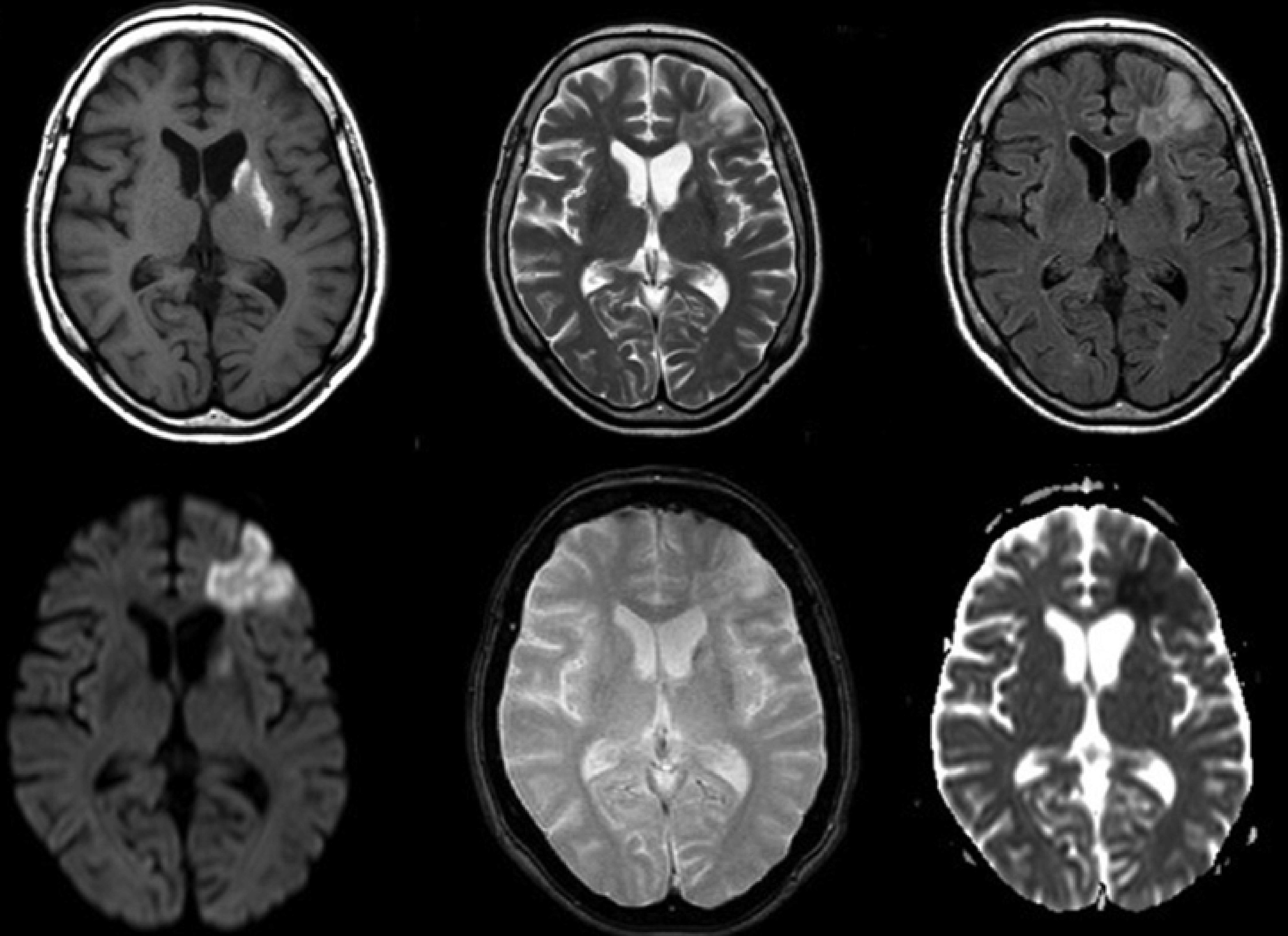
- Diagnosis algorithms - require large datasets
- Visualization - learn what to show, widely overlooked?
- **Segmentation** - outline, measure anatomy and pathology
- **Registration** - alignment for treatment planning, population analysis
- Acquisition - faster, better
- Abnormality detection - pathology
- Shape modelling
- Joint inference with other clinical data
- …

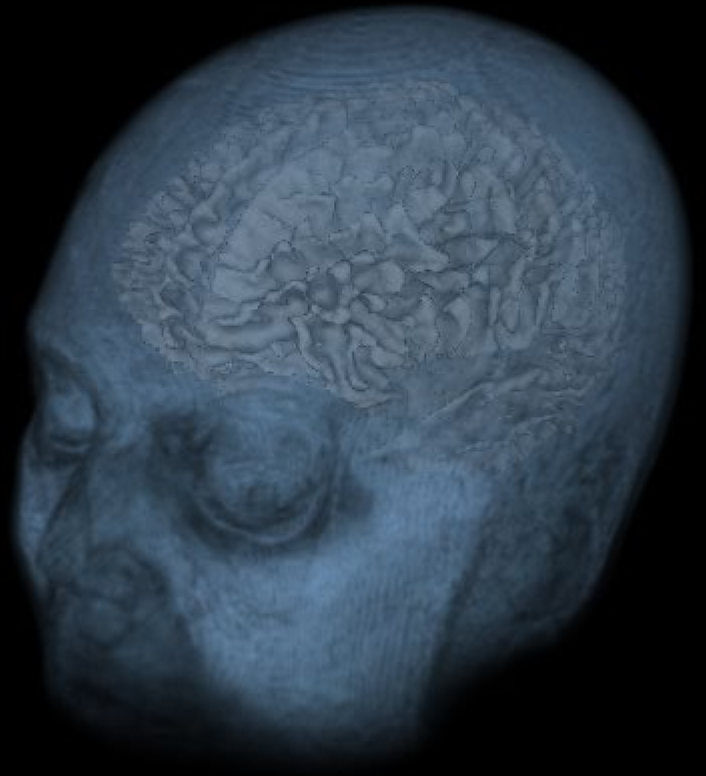
Properties of Medical Images

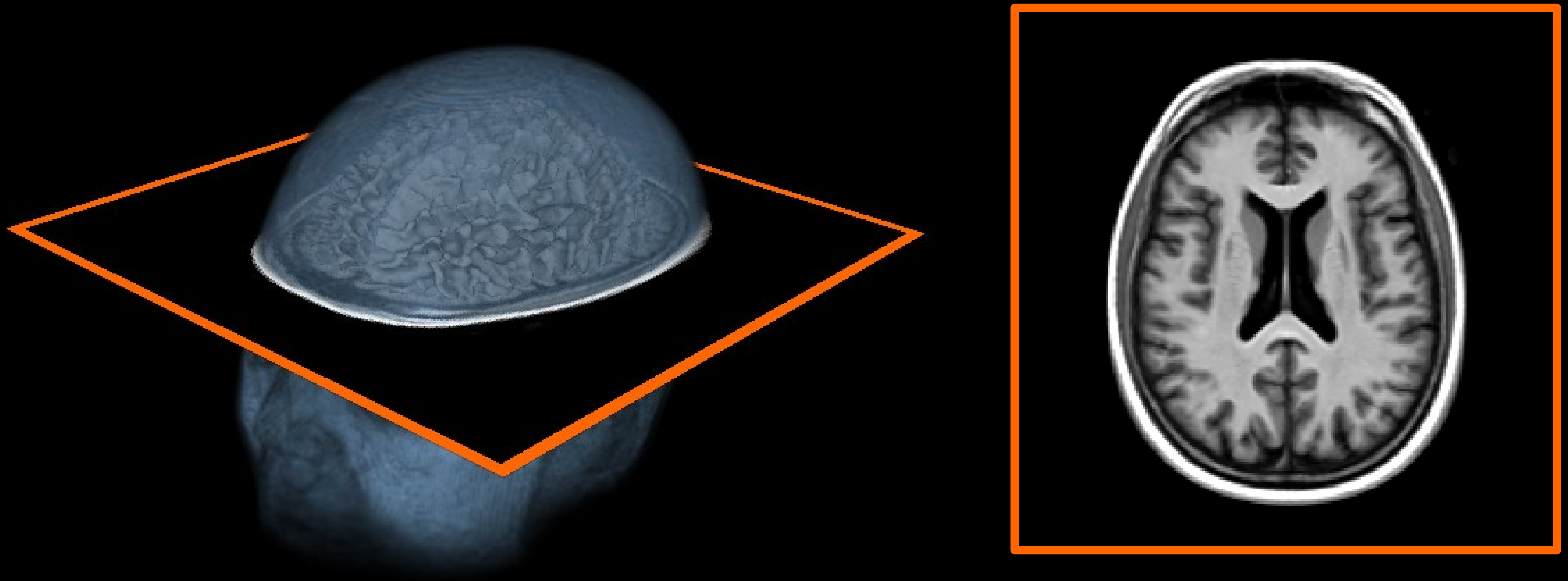
- Varies dramatically by image type

Fourier
Transform

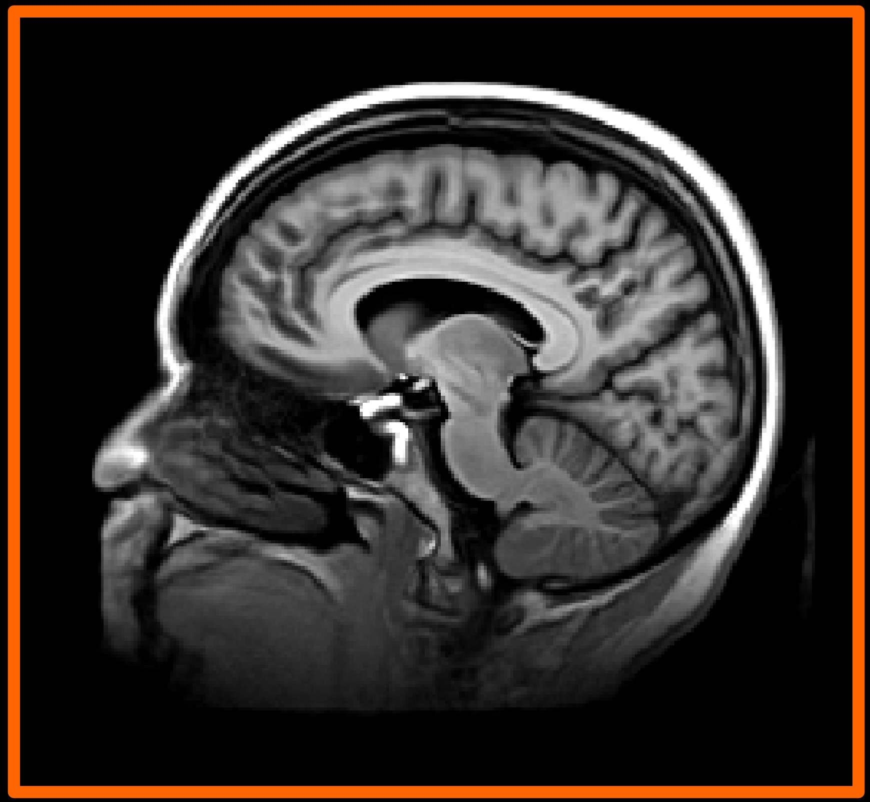




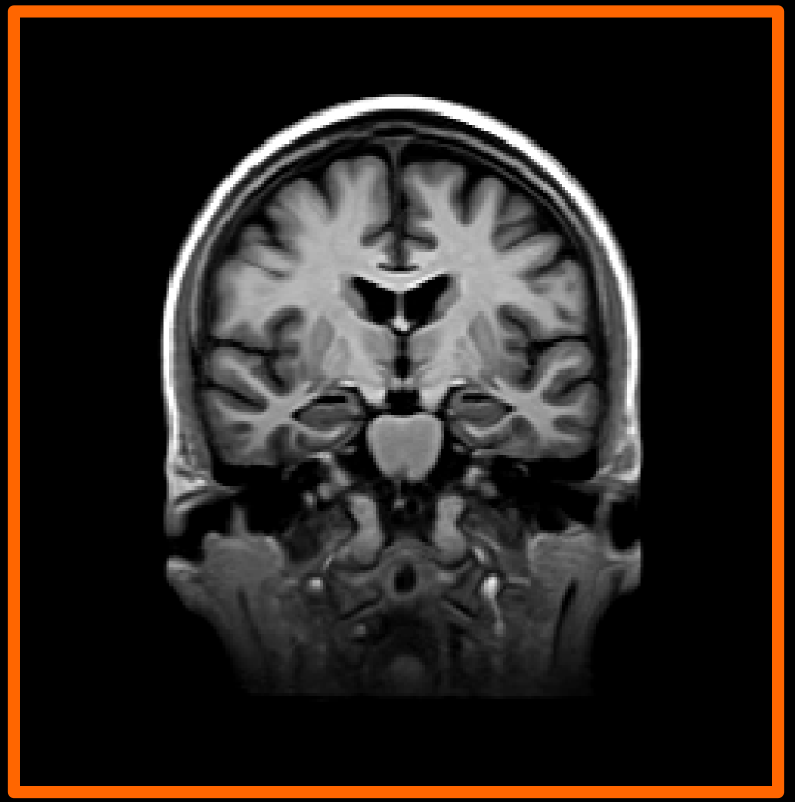




axial

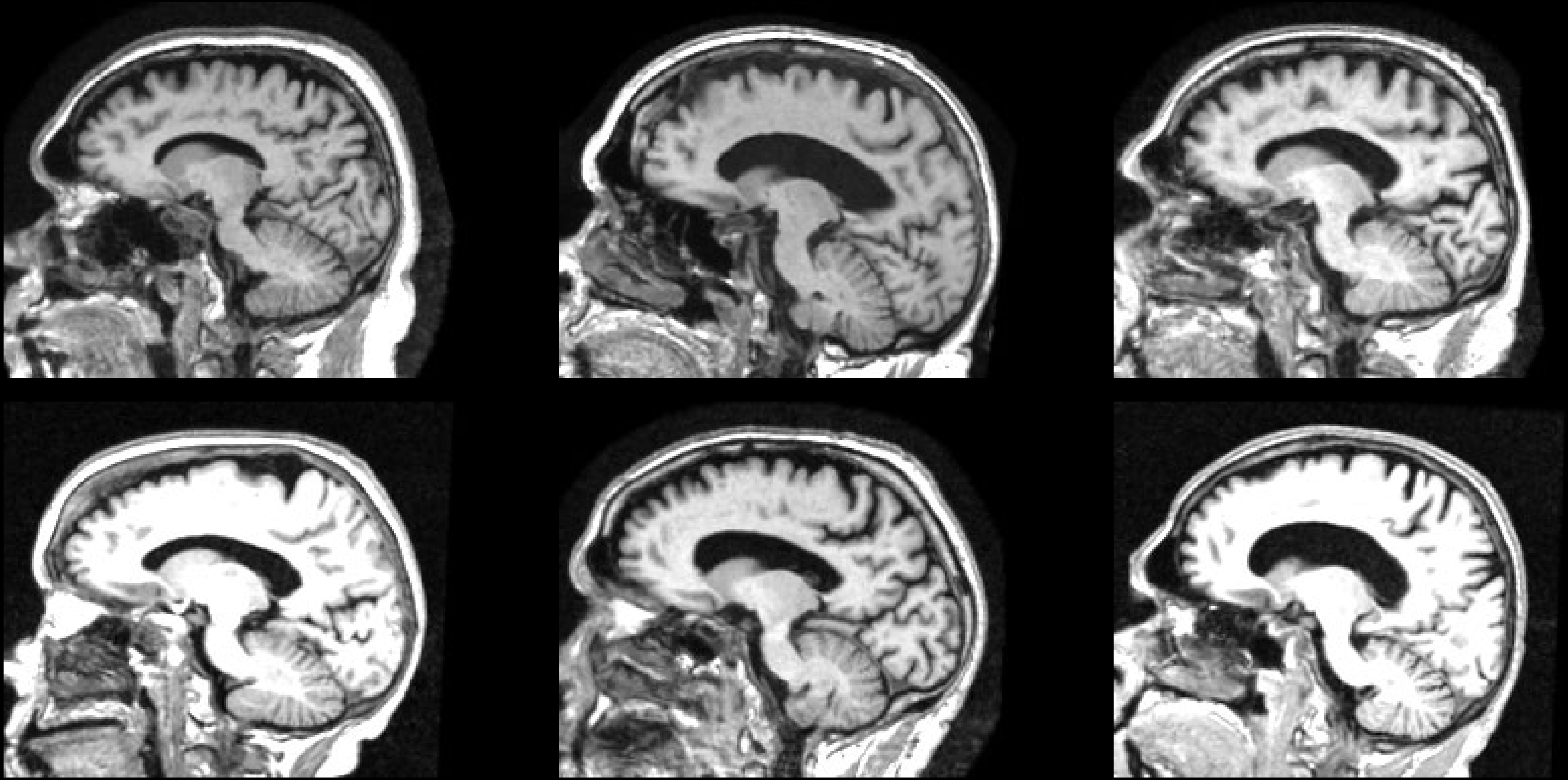


sagittal



coronal

Variability and similarity



Properties

- Vary dramatically by image type
- MR Image quality:
  - Different noise patterns, patient motion, disease, many modalities
- Commonality of anatomy
- Pathology (disease)
  - can be big and obvious (e.g. tumor)…
  - … or very small and subtle (e.g. neurodegeneration)
- A lot of 3+ dimensions
  - So ‘**voxel**’ (**volume element**) instead of ‘pixel’ (picture element)

Questions?

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- **Example: Segmentation**
  - ***Classical* and deep learning approaches**
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Image Segmentation

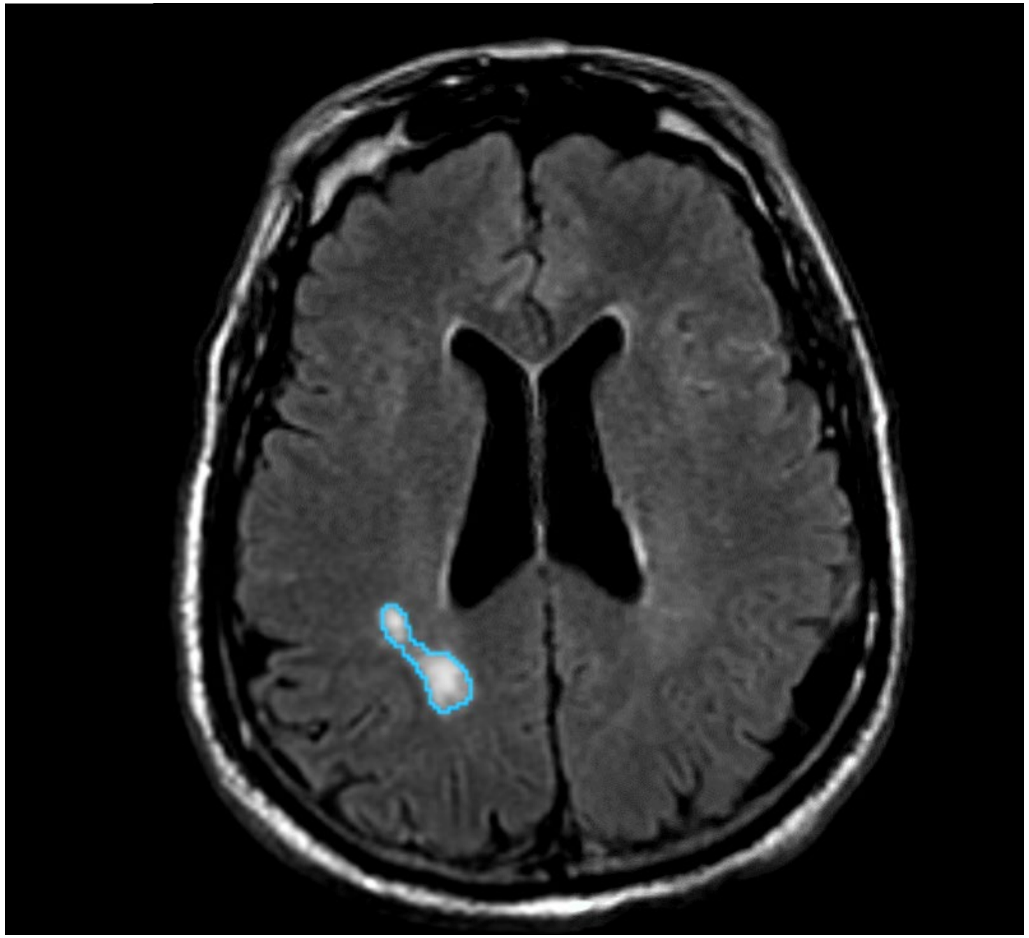
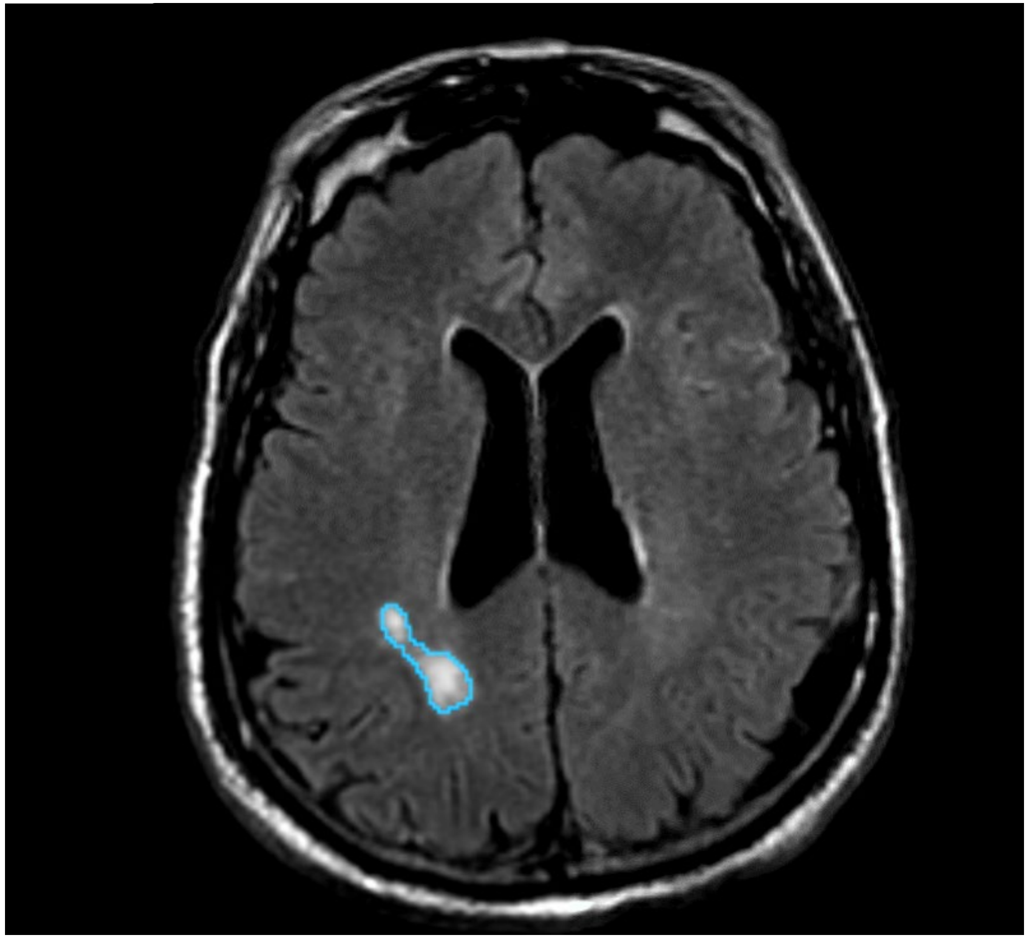
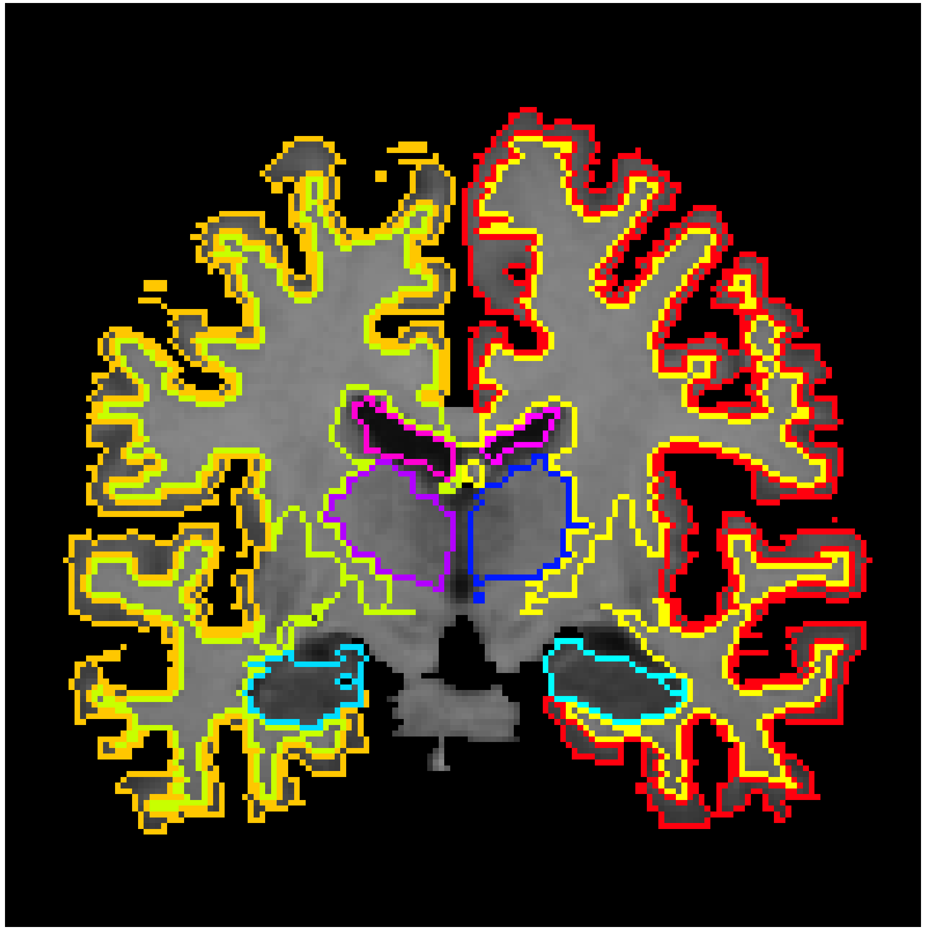
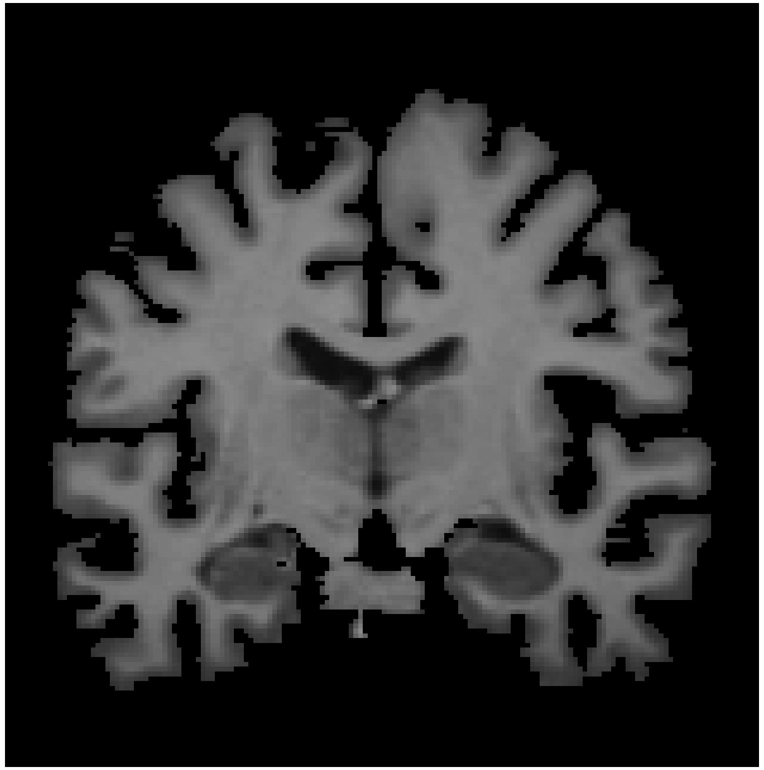


Image Segmentation

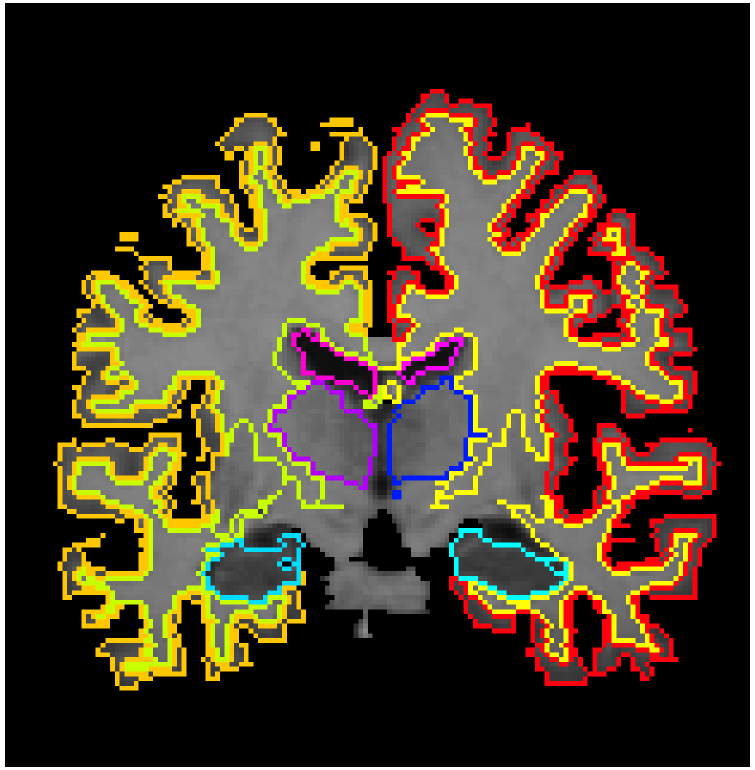




Supervised segmentation

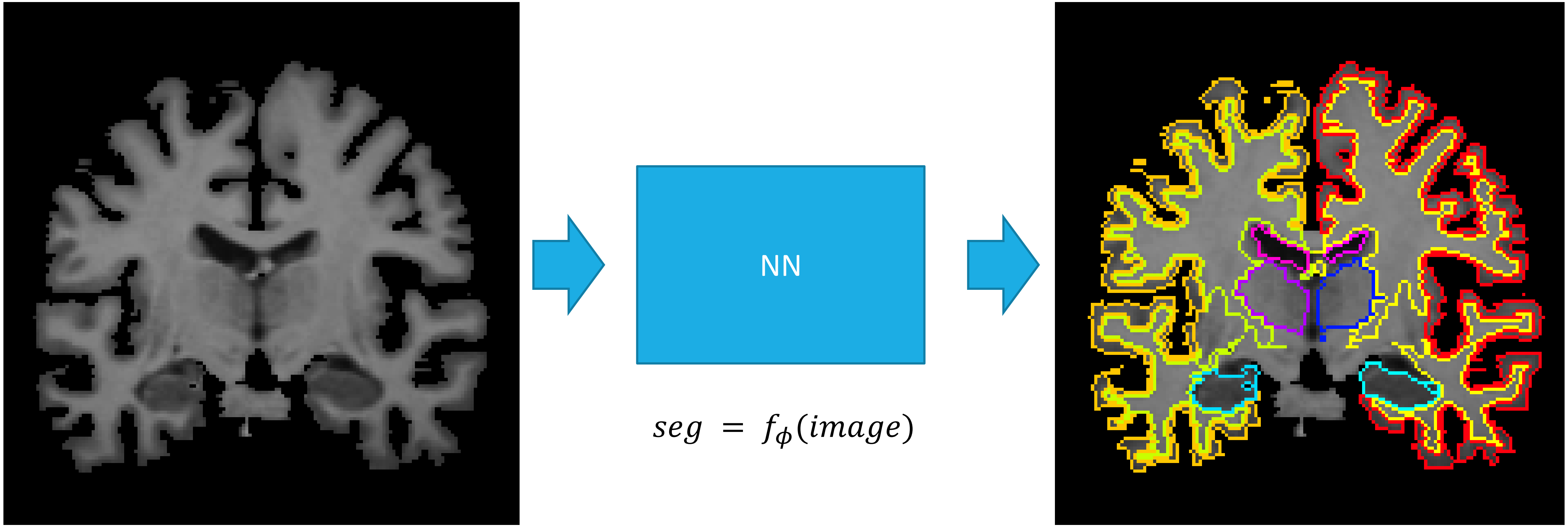


$$seg = f_{\phi}(image)$$



Supervised segmentation

Large example dataset: solved problem by DL?



$$seg \ = \ f_\phi(image)$$

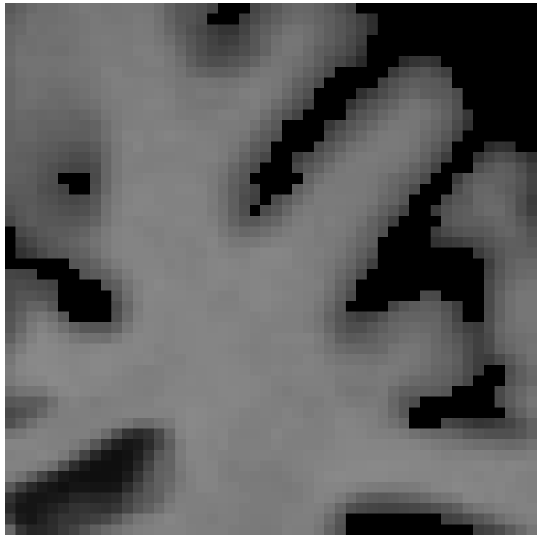
What kind of NN?

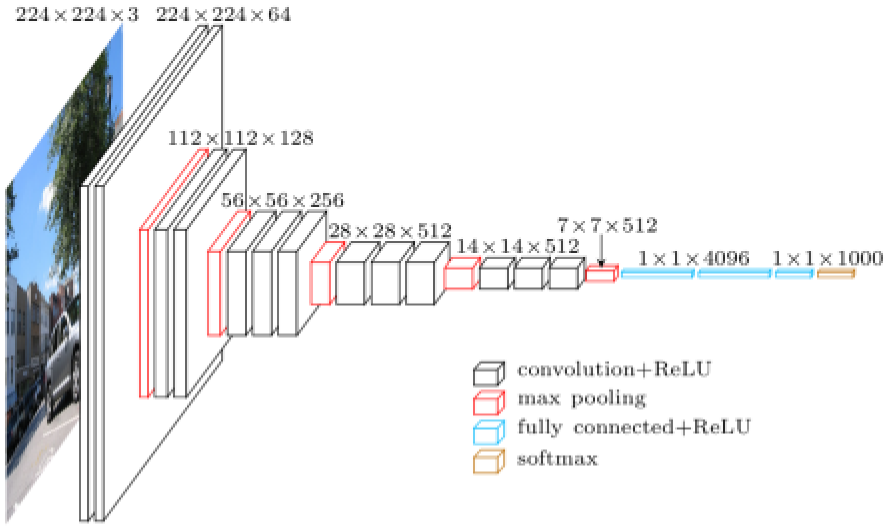
VGG, etc?

Use existing multi-label networks

Architecture: convolutions, max-pools, fully connected, etc.

But need to output 8 million voxels! – hours!





anatomical
label
(one-hot encoding)

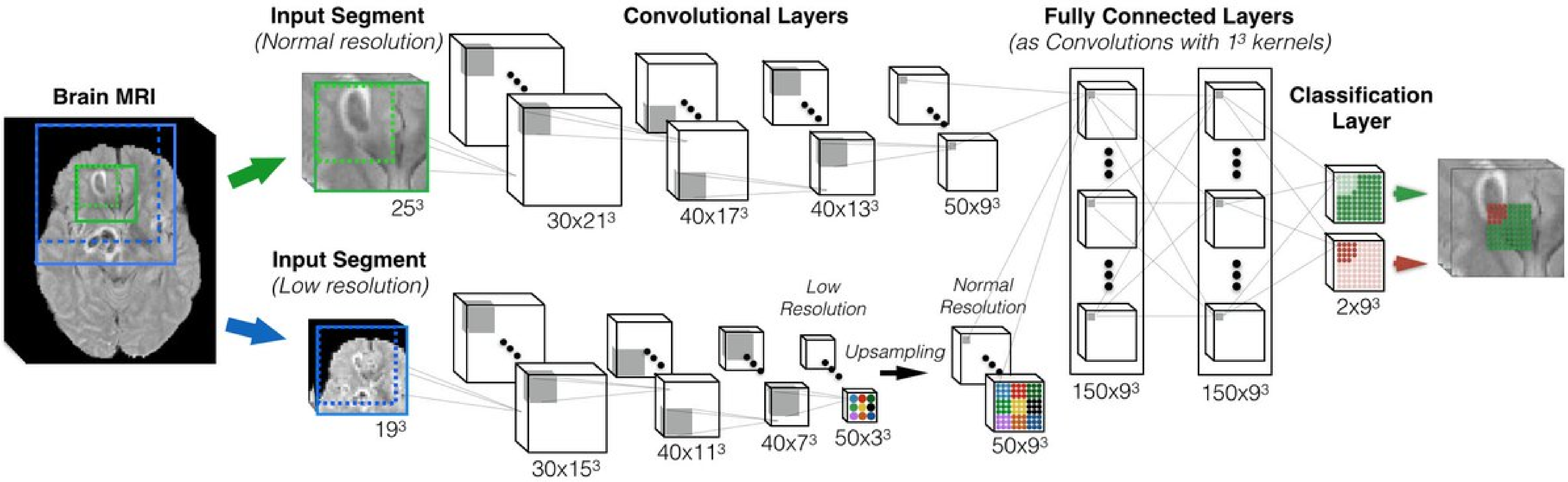
Fully convolutional?

Input-output both high dimensional, no max-pooling (make 3D)

10-layer network: don’t have enough context to predict anatomy

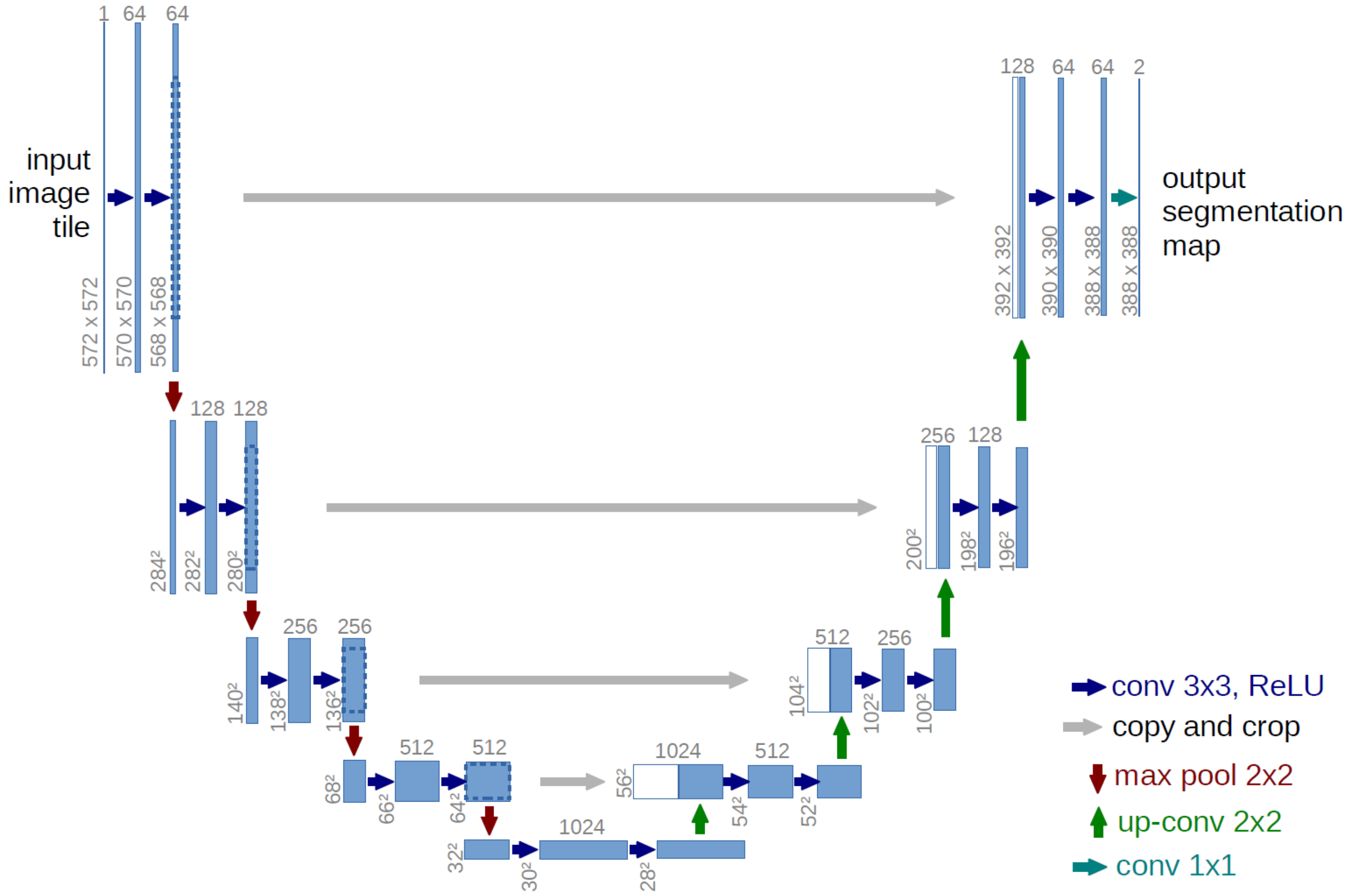
Deep networks (100 layers) – require too many parameters

Multi-scale inputs



Kamnitsas, et al., MedIA 2016

U-Net



Ronneberger et al, 2015

What kind of CNN?

Network architecture

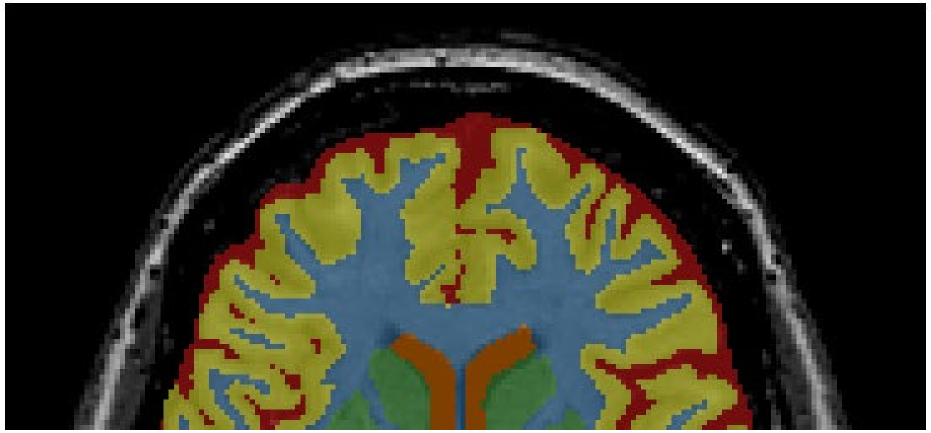
- Predict each voxel (e.g. 3D **VGG**)? too slow, cumbersome
- Fully Convolutional? Large memory, parameter space, not enough **field of view**
- Multiscale input?
- UNet!

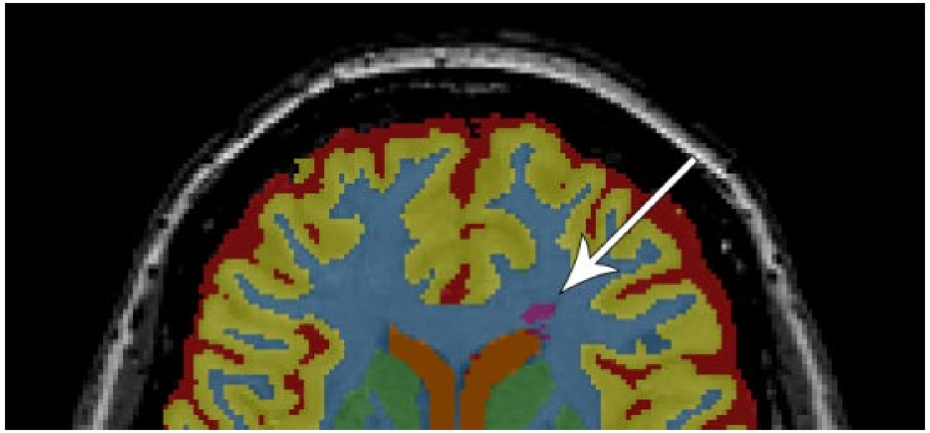
Results

Dice (Volume Overlap)	Dice (Volume Overlap)	Runtime
FreeSurfer (classical state of the art)	~80	~6-24 hours
Deep Methods	~85-91 (same data type)	~1 second-1 hour

Problems

- Often don’t actually have these **segmented** data
  - Long time to segment for experts!
  - Too many **modalities**
  - Too much variation (especially pathologies)
- Our metrics
  - Easy to compute, differentiate
  - Often not **anatomically** meaningful

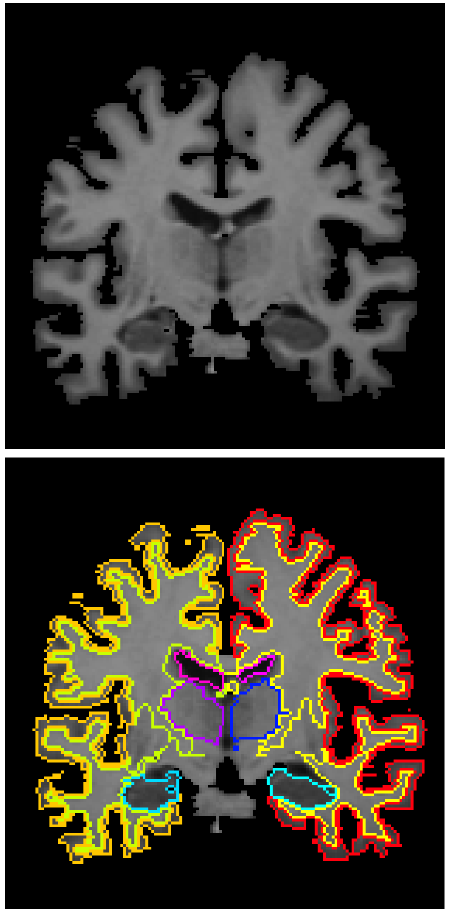


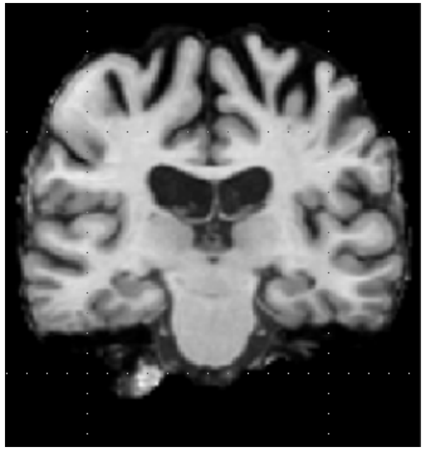


P. Moeskops et al, DLMIA, 2017

Segmentation in a more realistic setting

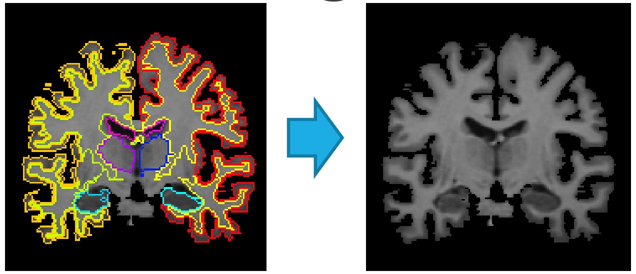
Few (one) segmented example

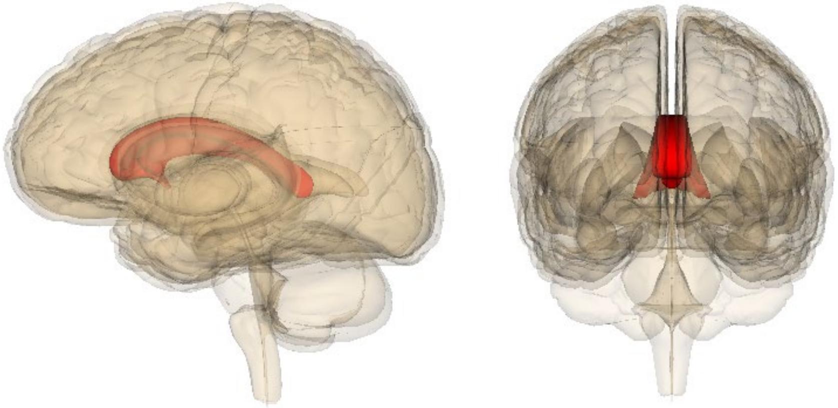




Probabilistic (Generative) Model

- Define segmentation -> image model $p(I|S) * P(S)$



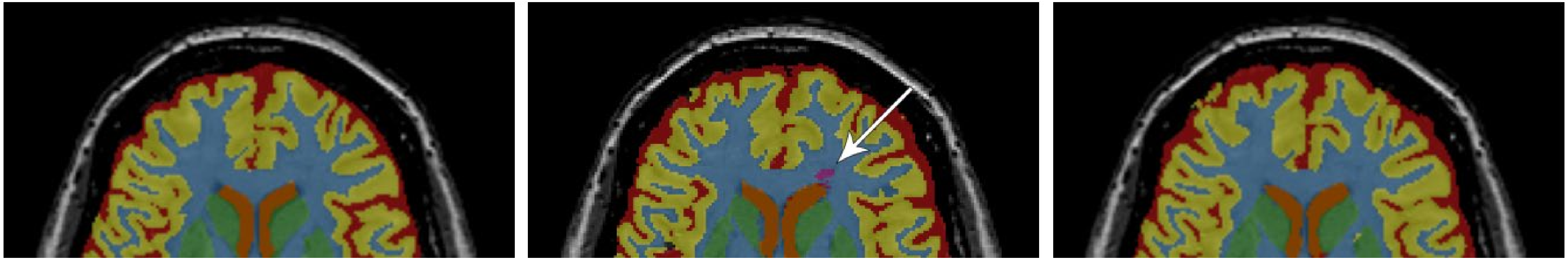


- Enables knowledge (priors) into segmentation model $p(S)$
  - $p(S)$ defined based on likely *shapes* of each label
  - $P(I|S)$ is the intensity (distribution) for each label
  - **Inference**: $p(S|I)$ at each voxel: **label** matches the **intensity** such that **shapes** make sense.

Probabilistic (Generative) Model

- Combine with deep learning predictions:

  p(S) can be anatomically specified
  or learned from another distribution
- Attach prior to network, or modelling through VAEs, etc…



P. Moeskops et al, DLMIA, 2017

Brains (anatomy) are similar!

- Can similarity of brains help?

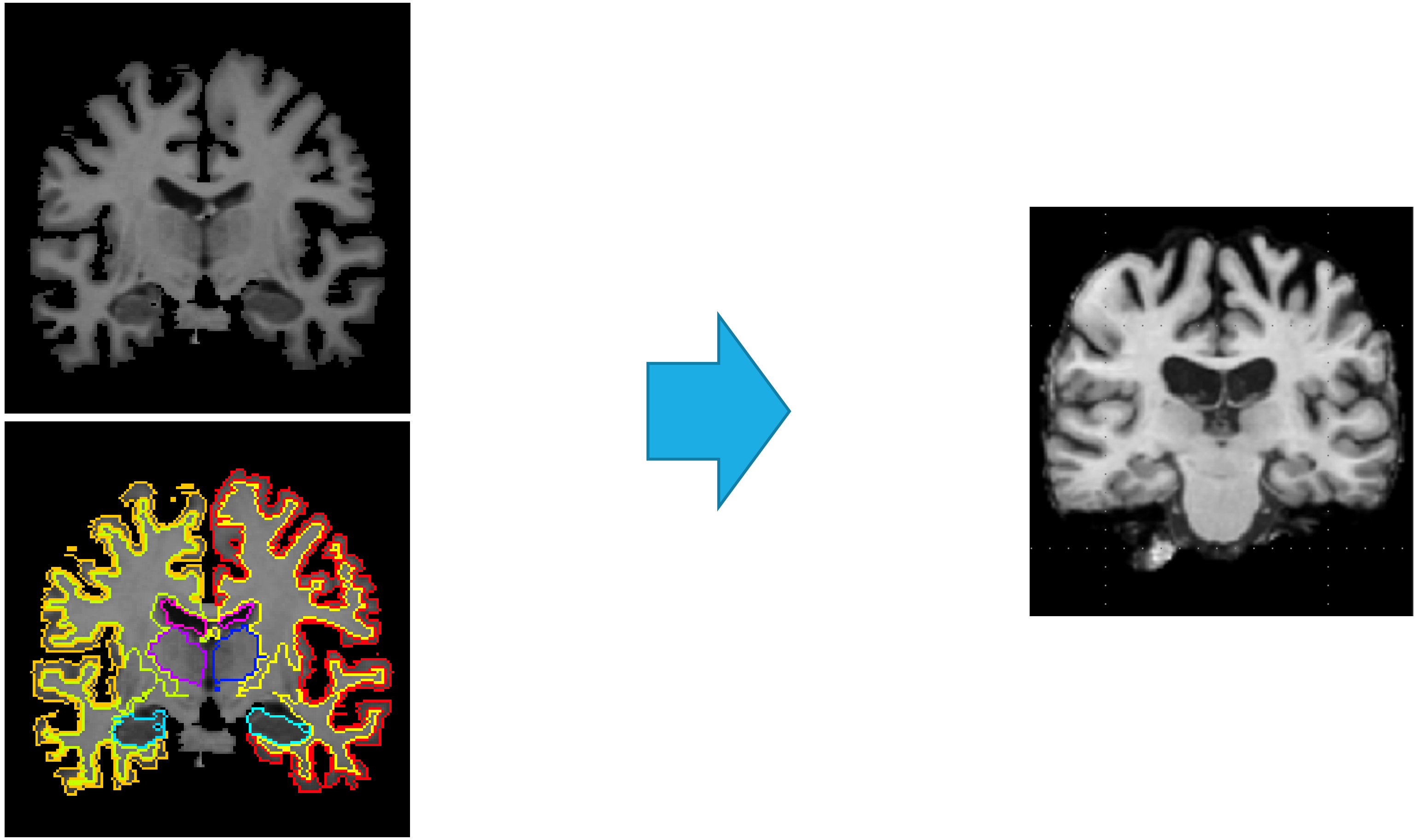


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Image Registration

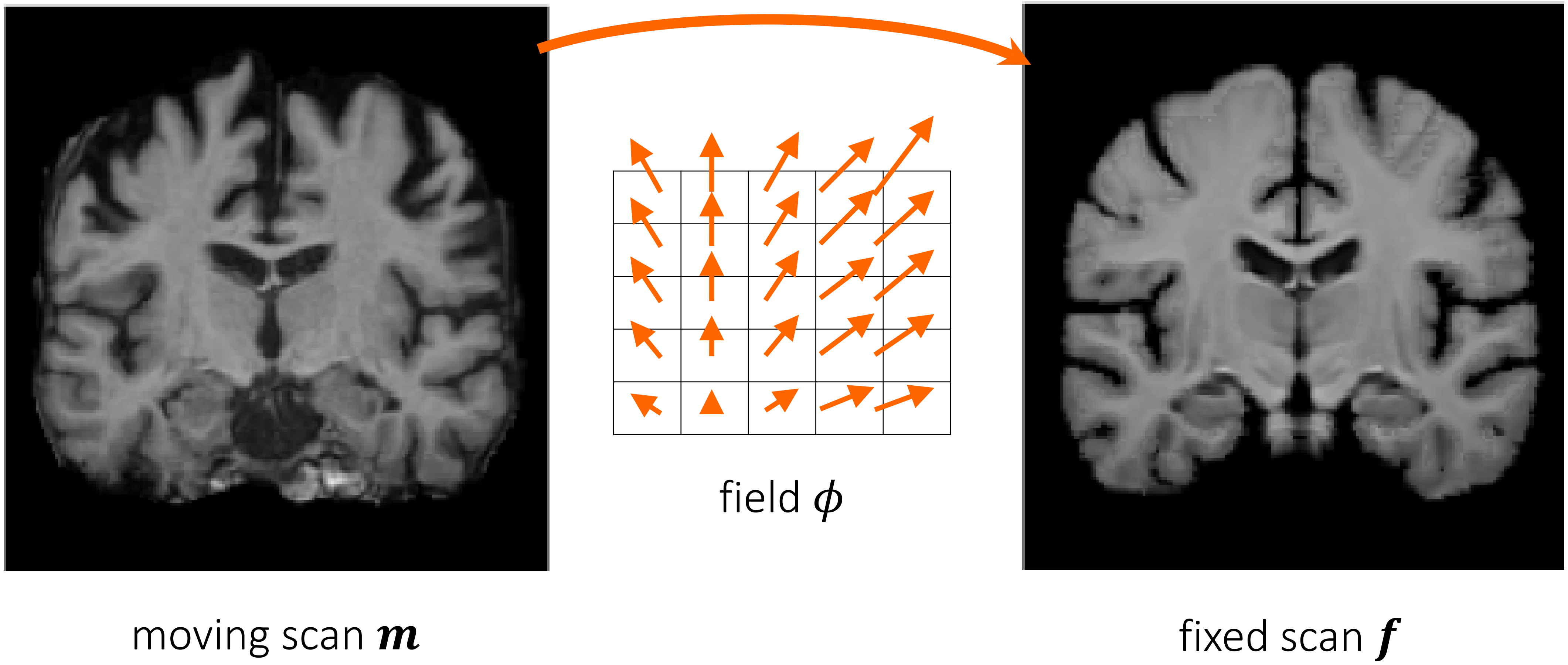
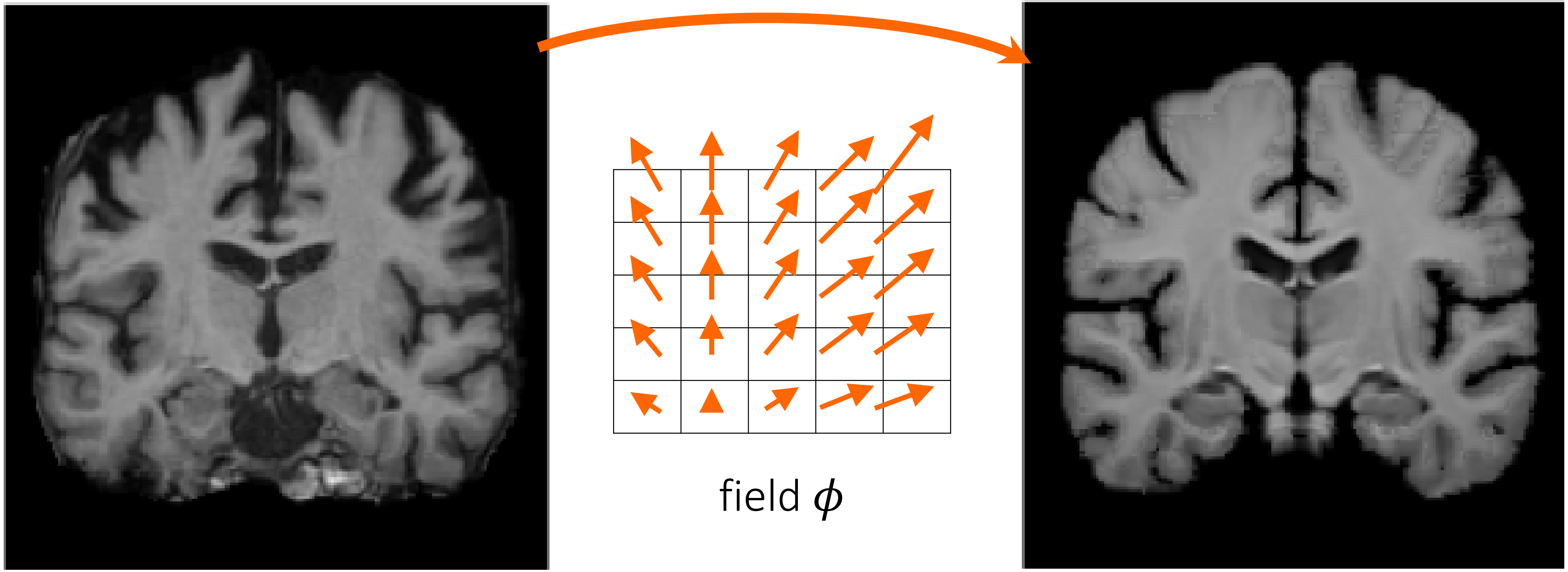


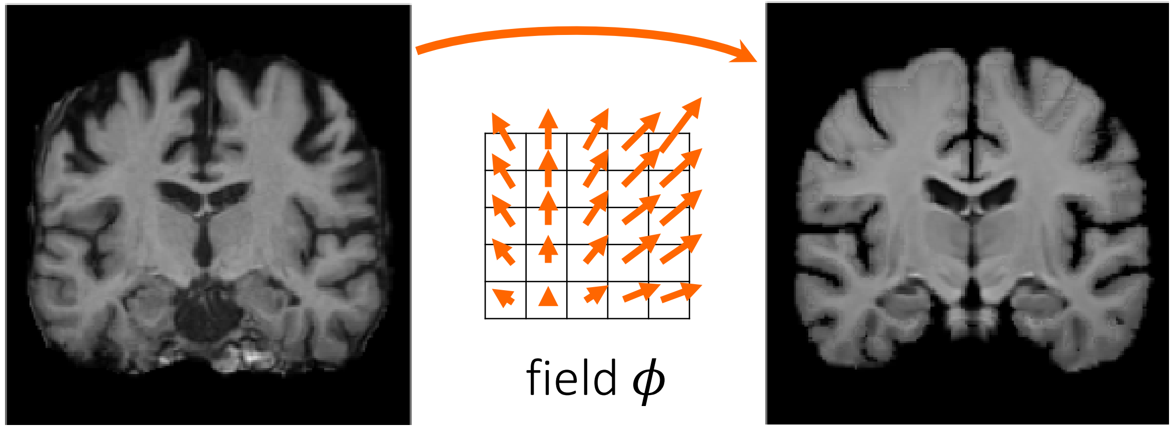
Image Registration



moving scan $\boldsymbol{m}$ fixed scan $\boldsymbol{f}$

Traditional approach

scan $\boldsymbol{m}$



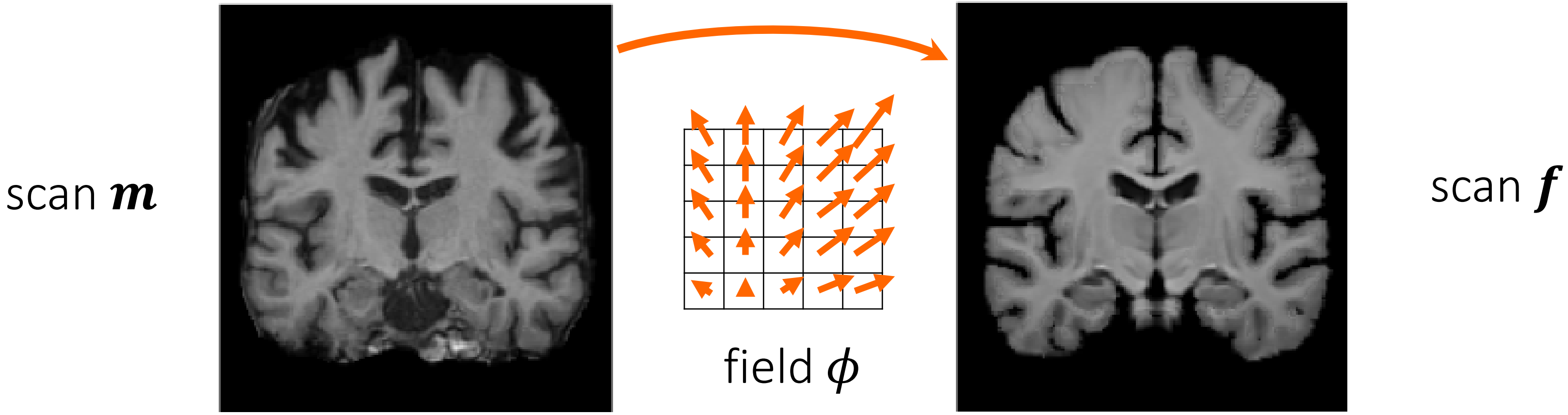
scan $\boldsymbol{f}$

warped scan m

$$\hat{\phi}_{m,f} = argmin_{\phi} \; \underbrace{||m \circ \phi - f||}_{\text{images match}}$$

optimal deformation field

Traditional approach

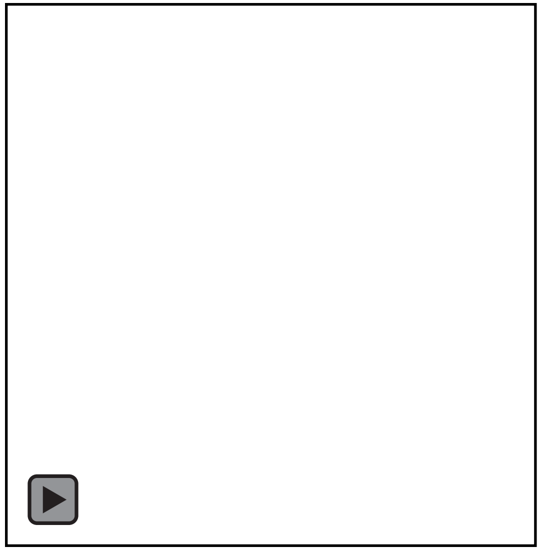


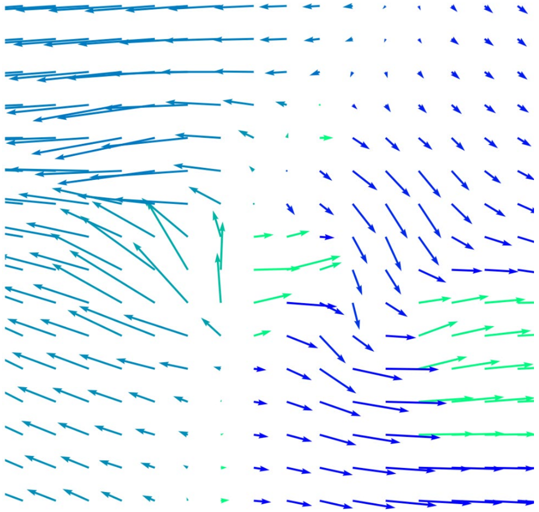
warped scan m

$$\underset{\text{optimal deformation field}}{\hat{\phi}_{m,f}} = argmin_{\phi} \; \underbrace{\|m \circ \phi - f\|}_{\text{images match}} + \lambda \, \underbrace{\|\nabla \phi\|}_{\text{Anatomically smooth}}$$

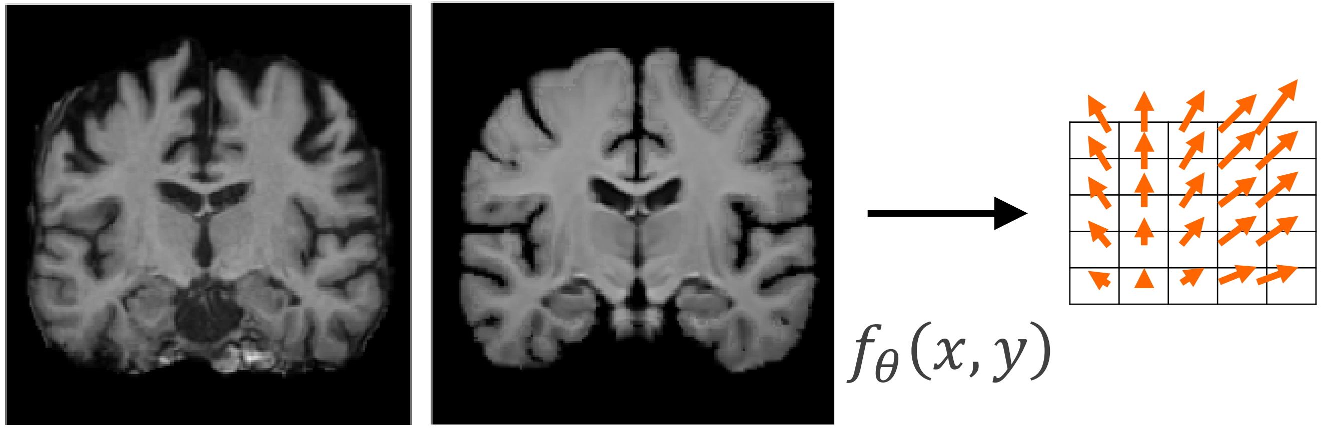
Pairwise optimization: slow (hours per image on CPU)

Animation





How can machine learning help?

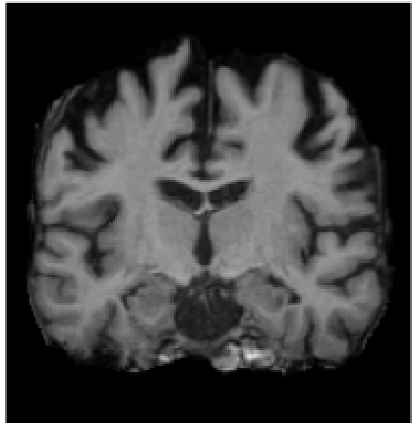


$f_\theta(x, y)$

scan $\boldsymbol{y}$ scan $\boldsymbol{x}$ field $\boldsymbol{\phi}$

Balakrishnan CVPR 2018, IEE TMI 2019
Dalca MICCAI 2018, MedIA 2019, CHIL 2020

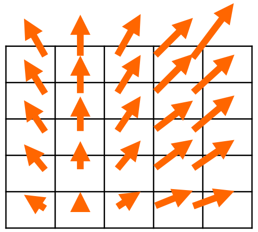
Supervised Learning



scan $\boldsymbol{y}$

scan $\boldsymbol{x}$

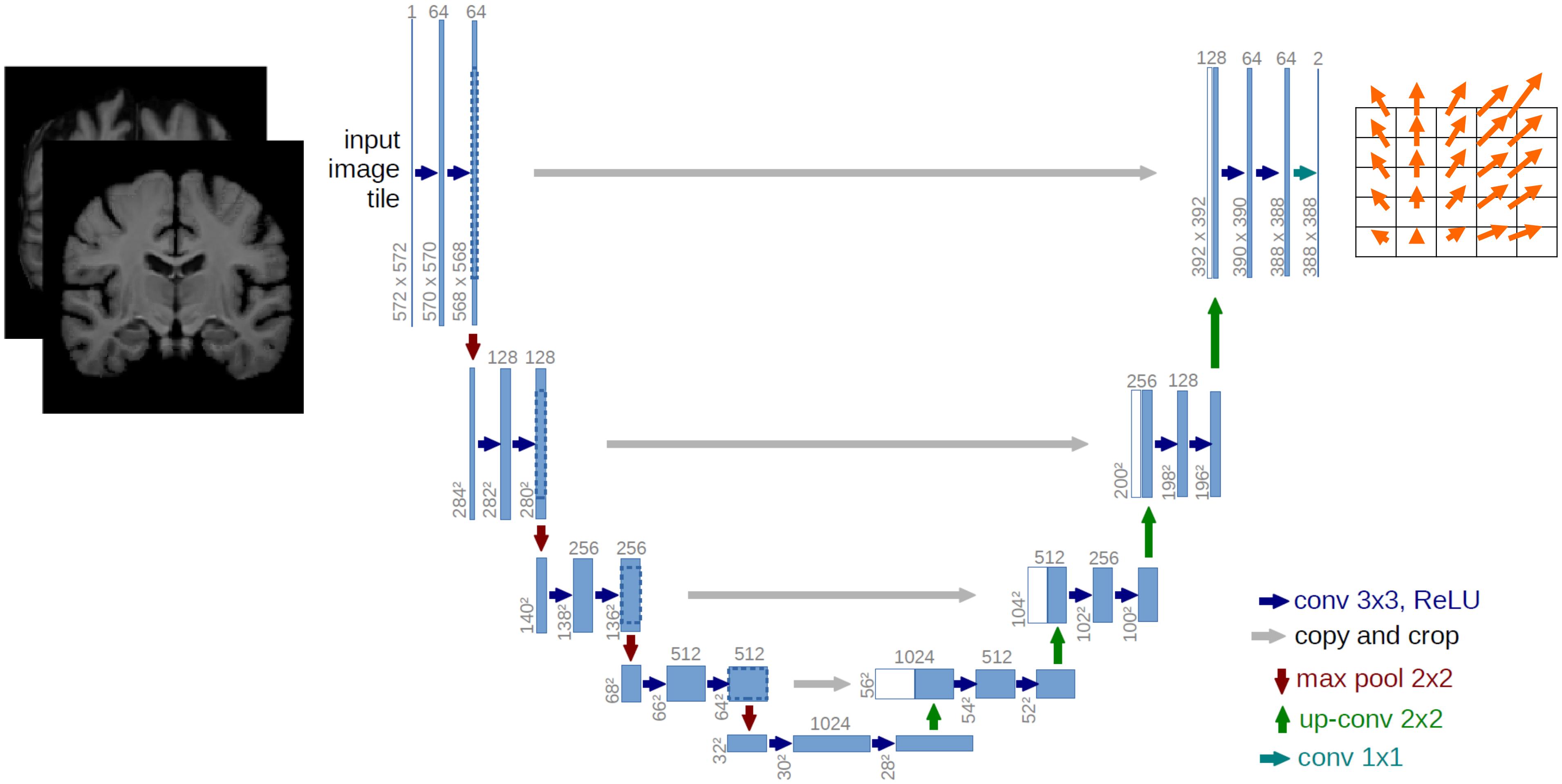
$f_\theta(x, y)$



field $\boldsymbol{\phi}$

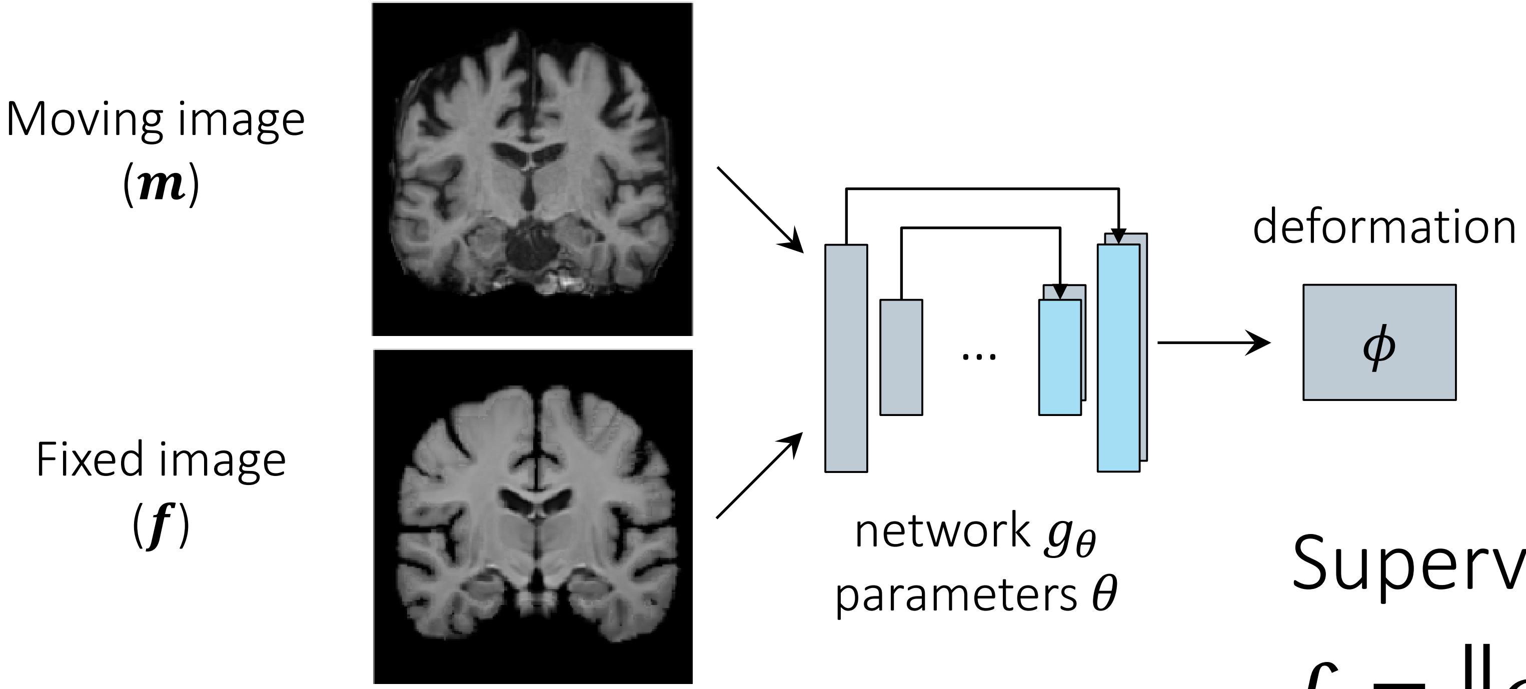
fast for new image pair!

What kind of architecture?



Ronneberger et al, 2015

Framework Loss



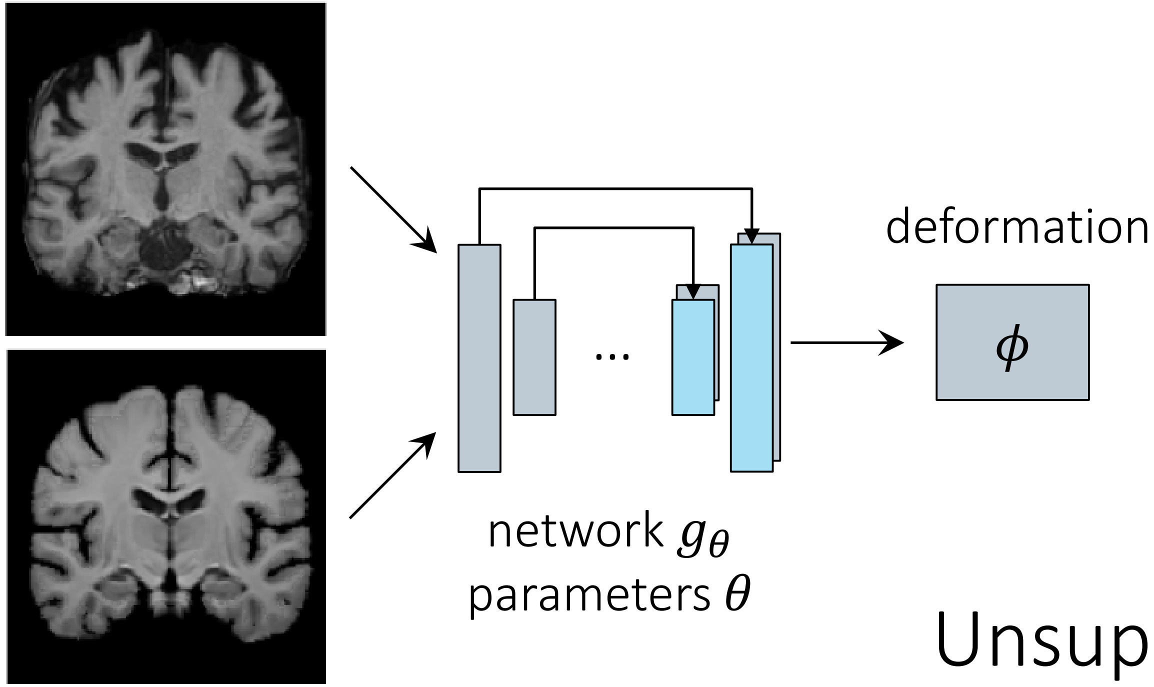
Supervised:

$$\mathcal{L} = \left\|\phi - \phi_{gt}\right\|^2$$

Framework Loss

Moving image
($\boldsymbol{m}$)

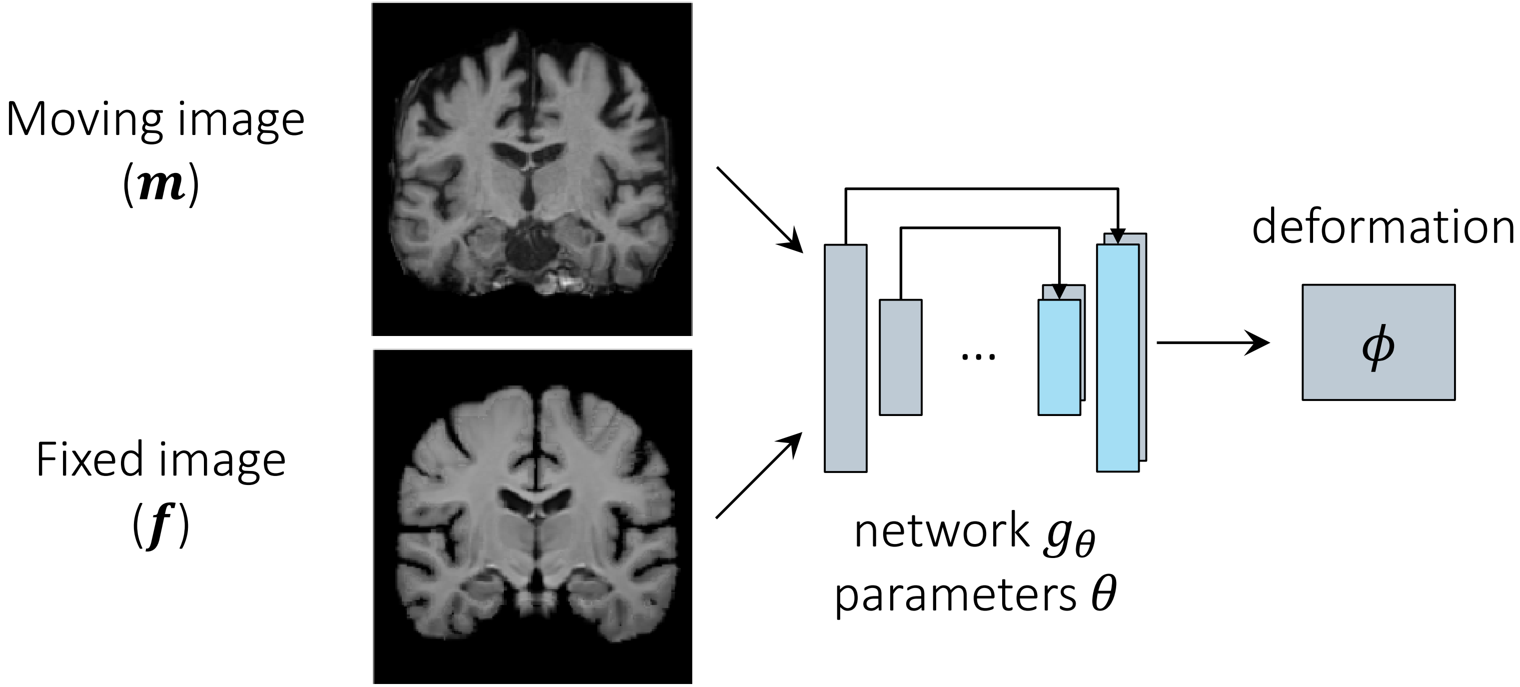
Fixed image
($\boldsymbol{f}$)



Unsupervised:

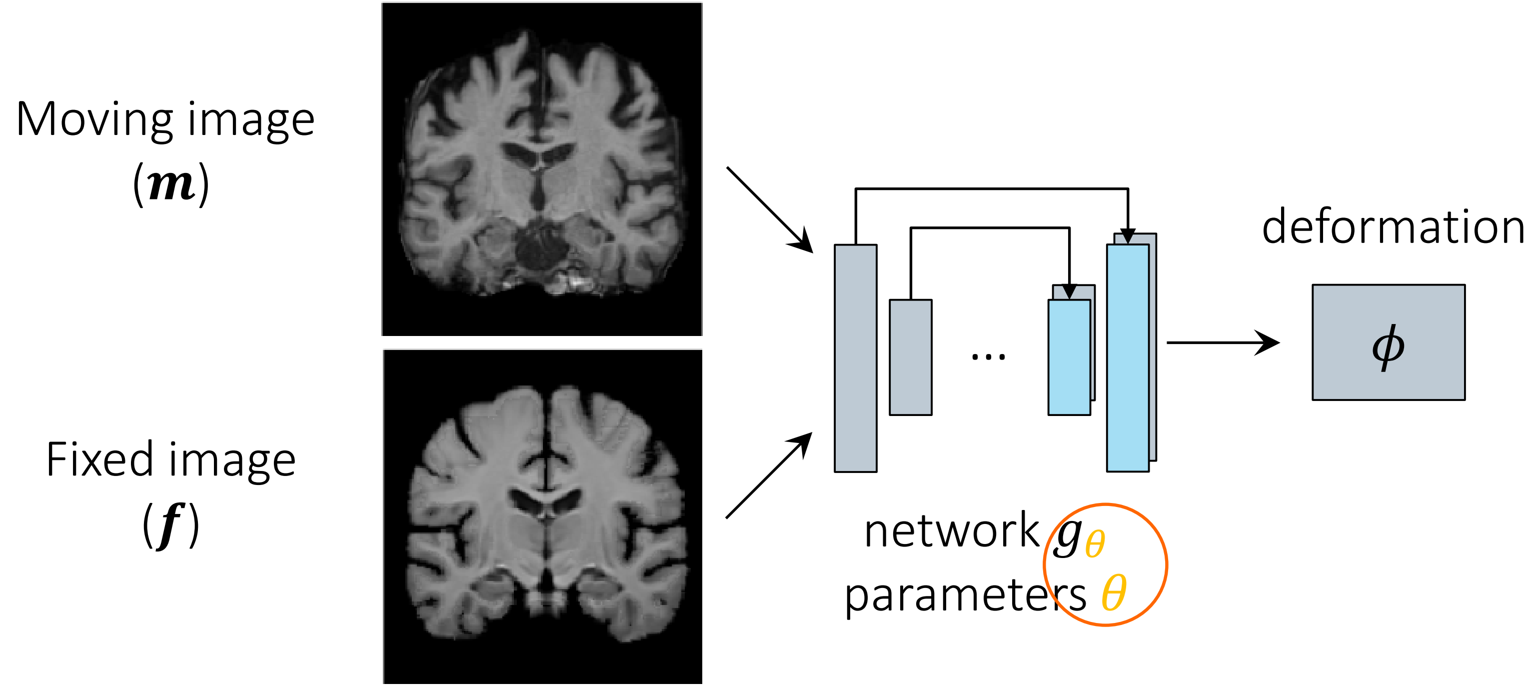
$$\mathcal{L} = \|m \circ \phi - f\| + \lambda \,\mathrm{Reg}(\phi)$$

Framework Loss



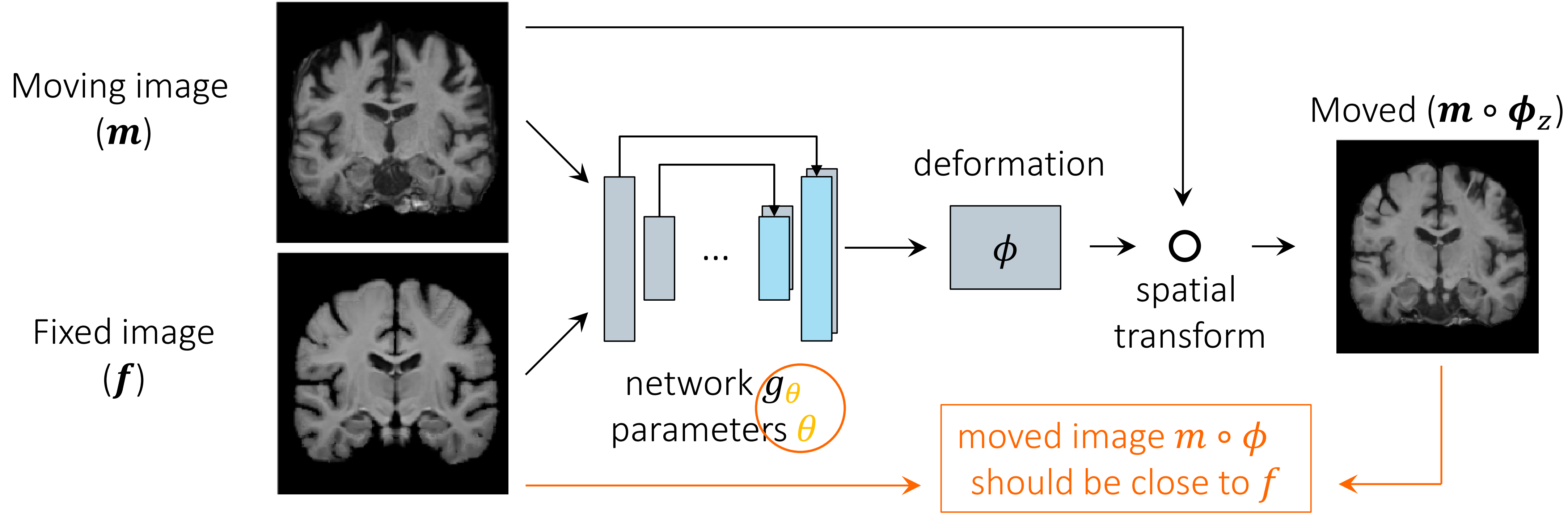
$$\mathcal{L} = \sum_{i,j} \|m_i \circ \phi_{ij} - f_j\| + \lambda \,\mathrm{Reg}(\phi_{ij})$$

Framework Loss



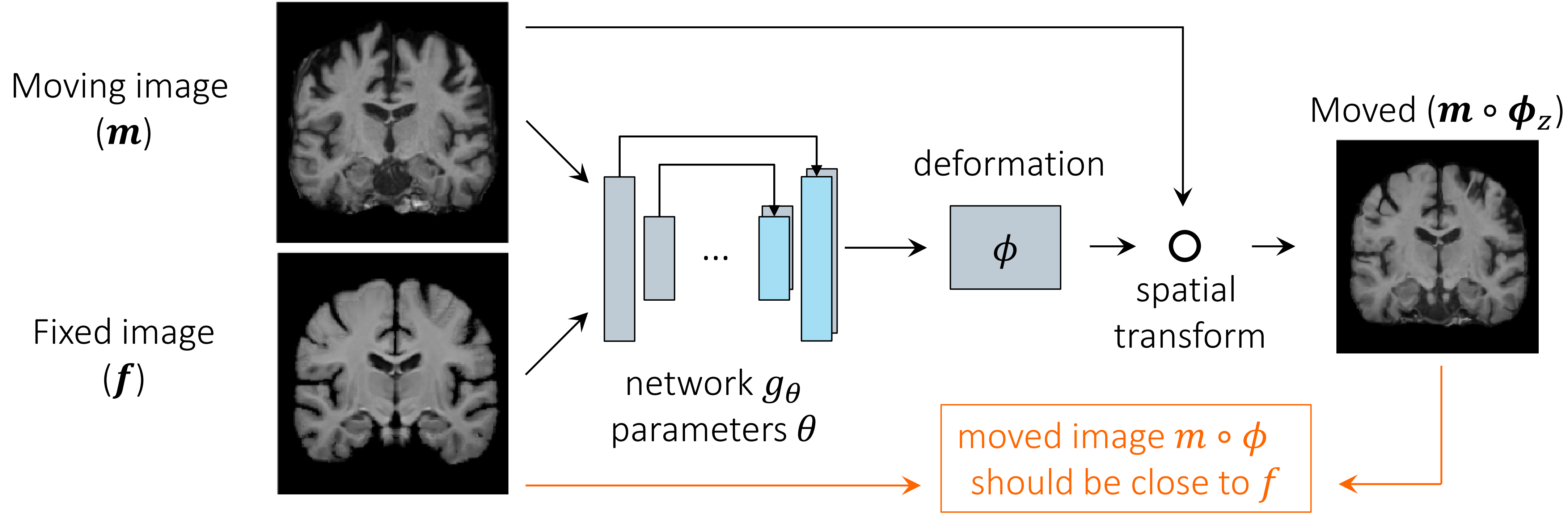
$$\mathcal{L}(\theta;\mathrm{data}) = \sum_{i,j} \| m_i \circ \underbrace{g_\theta(m_{i.}\, f_i)}_{\phi_{ij}} - f_{ij} \| + \lambda\, \mathrm{Reg}(\underbrace{g_\theta(m_{i.}\, f_i)}_{\phi_{ij}})$$

Framework Loss



$$\mathcal{L}(\theta; \text{data}) = \sum_{i,j} \| m_i \circ \underbrace{g_\theta(m_{i.} f_i)}_{\phi_{ij}} - f_{ij} \| + \lambda \operatorname{Reg}(\underbrace{g_\theta(m_{i.} f_i)}_{\phi_{ij}})$$

Training

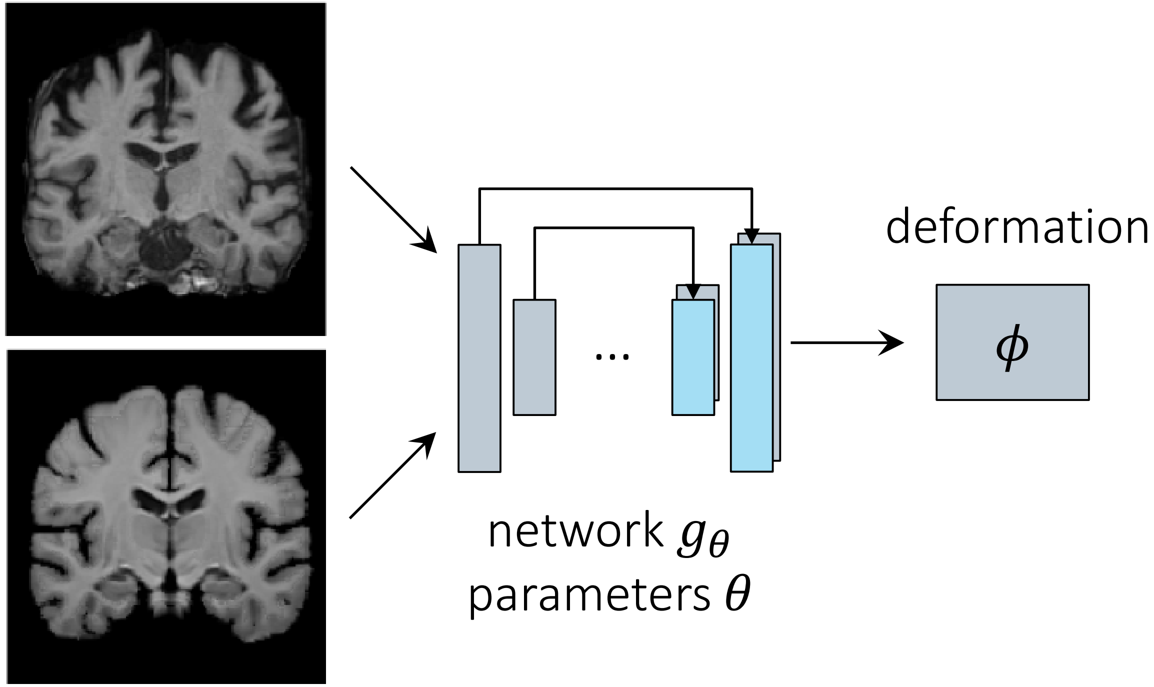


- SGD based techniques
- Each image pair contributes **slightly** to θ
  Classical optimization: slightly update ϕ for an image pair

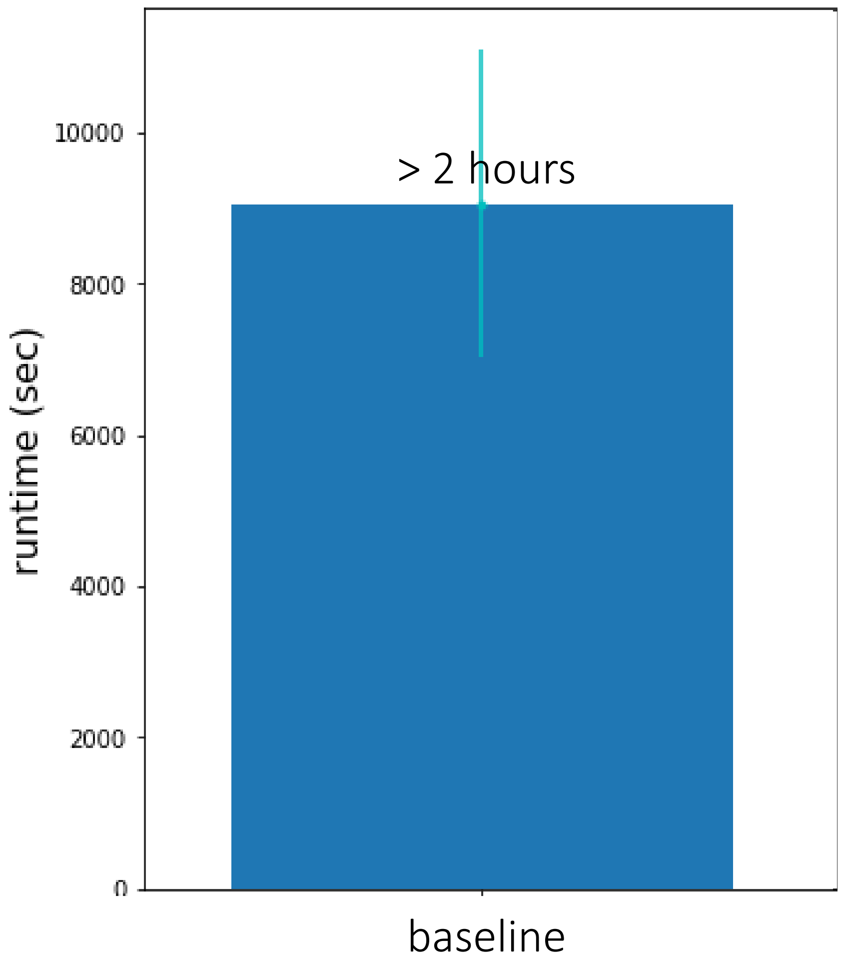
Registration

Moving image
($\boldsymbol{m}$)

Fixed image
($\boldsymbol{f}$)



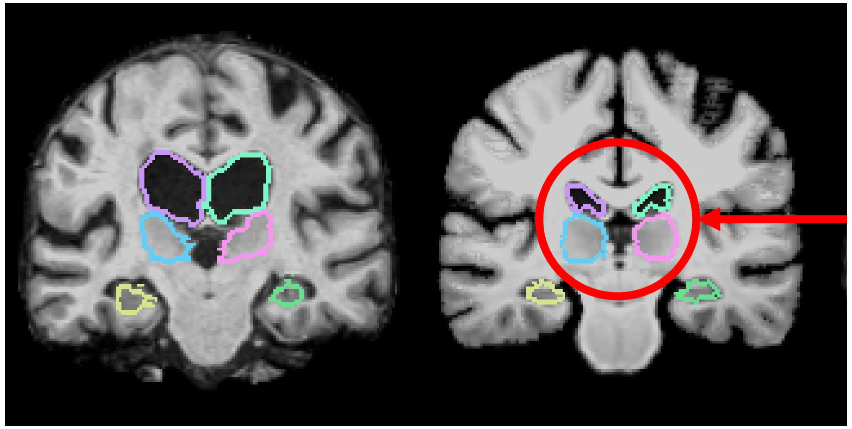
Runtime for a new 3D image pair



How to evaluate?

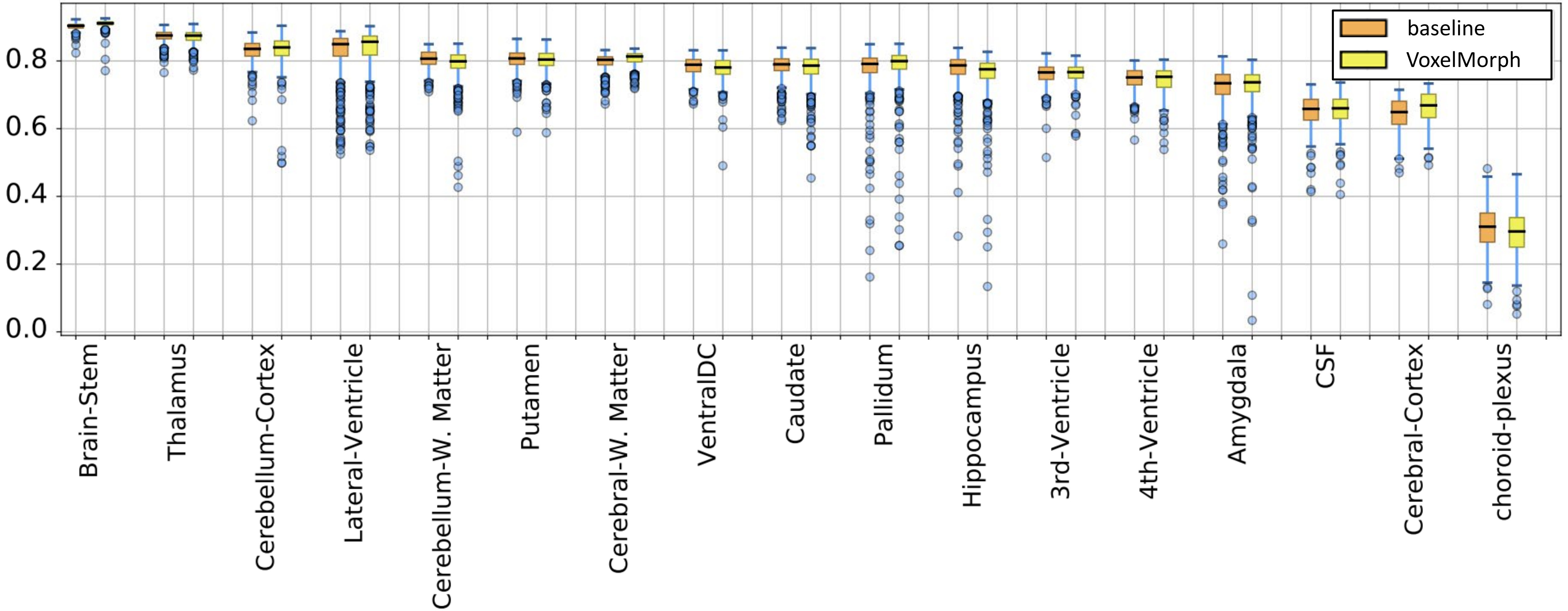
scan m scan f

pair 1



*algorithms only see images, no segmentation maps

Accuracy via volume overlap (Dice)



Remarks

- We derive network probabilistically **from probabilistic model**
  - $p(m|\phi; f) * p(\phi) \rightarrow p(\phi|m; f)$
  - Variational approximation to $p(\phi|m; f)$ leads to network

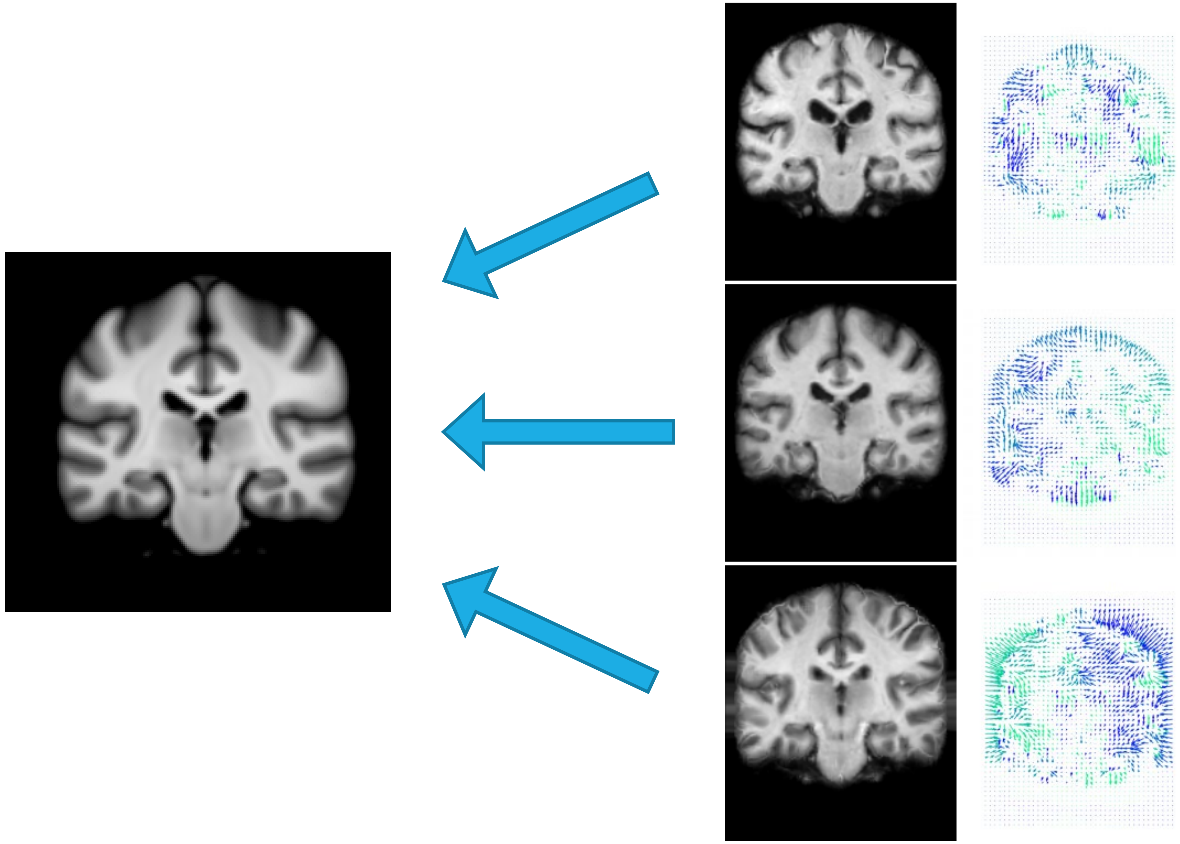
- Can impose stricter anatomical consistency (**diffeomorphisms**)
  - Provide topological guarantees

- Can use segmentations during training if we have them.

Dalca et al, MICCAI 2018; MedIA 2019

Questions?

Registration usecase: ADNI deformations



8000 scans

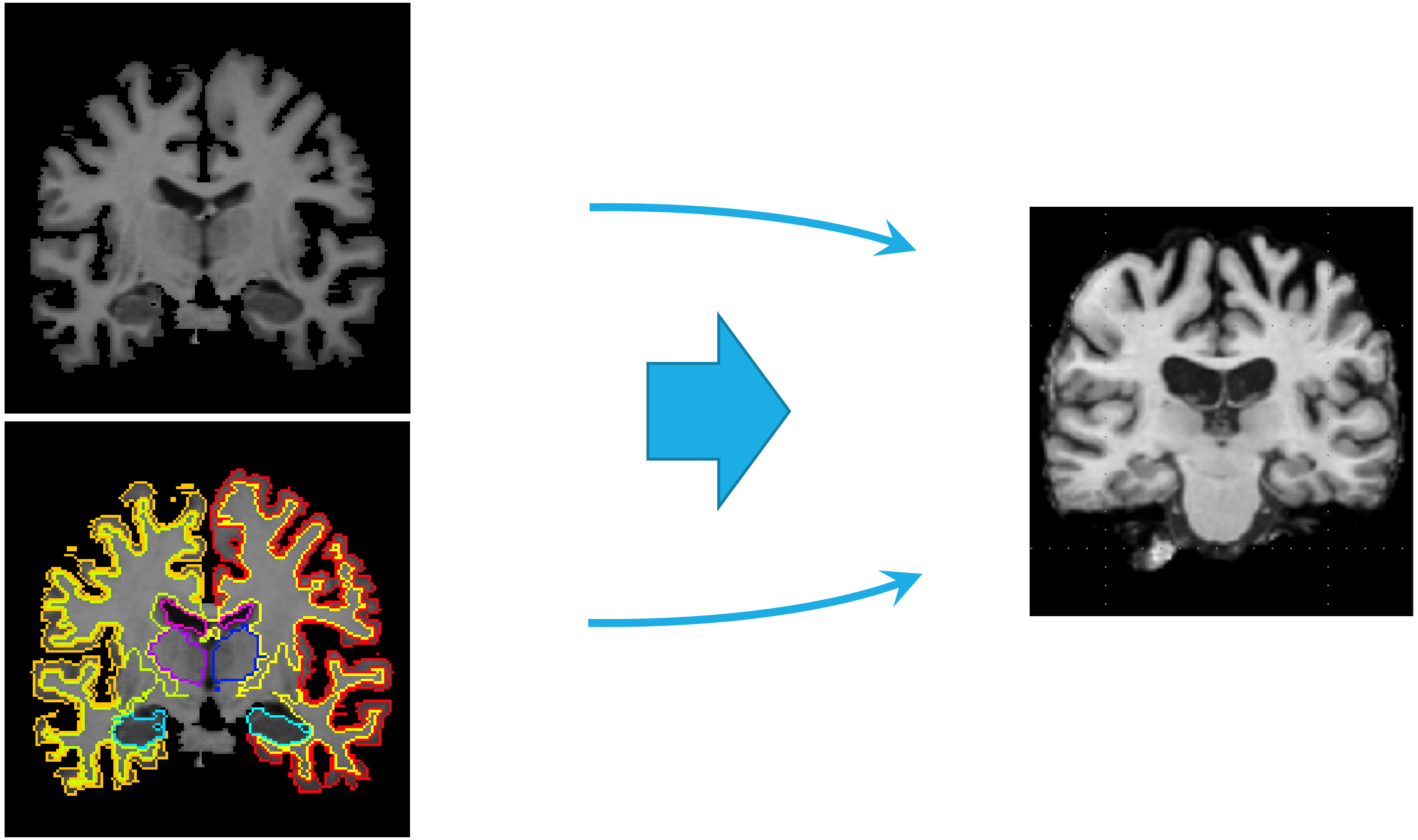
Analyze deformation fields

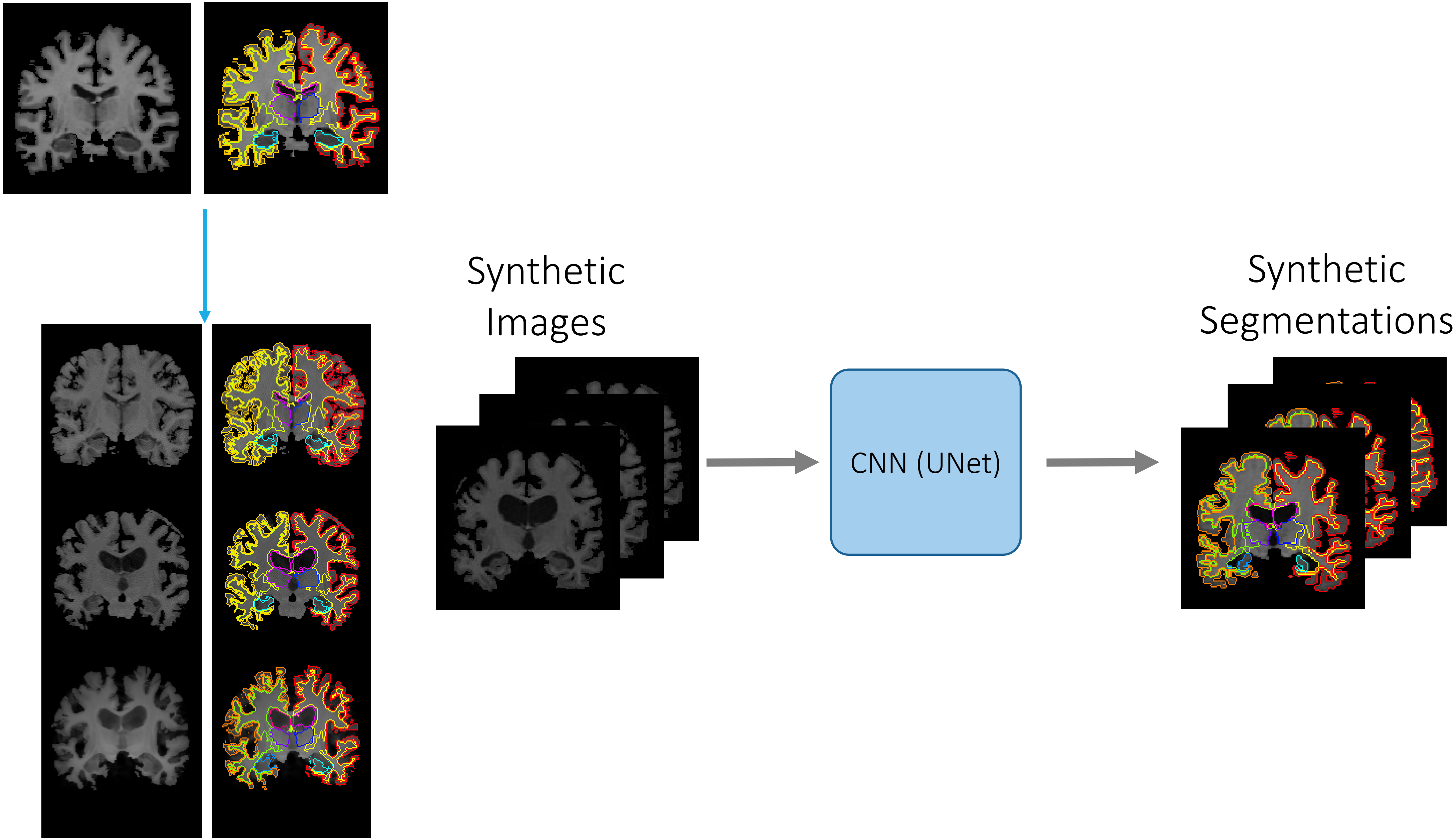
Example:
Anatomical variability
vs genetics

PhD: weeks on cluster
Now: 2 hours on 1 GPU

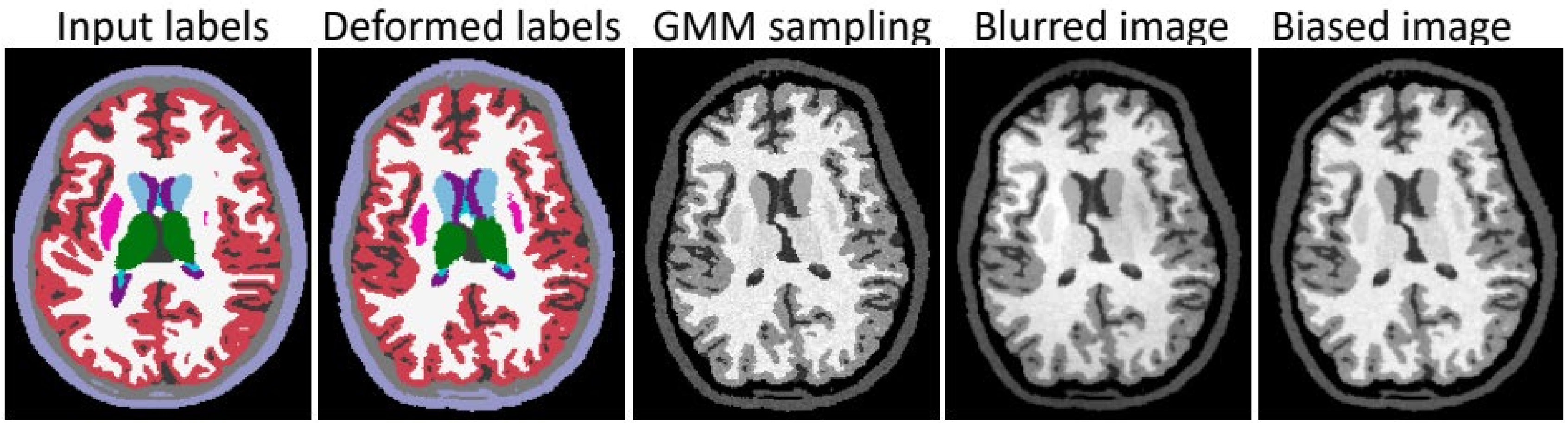
Registration usecase: segmentation

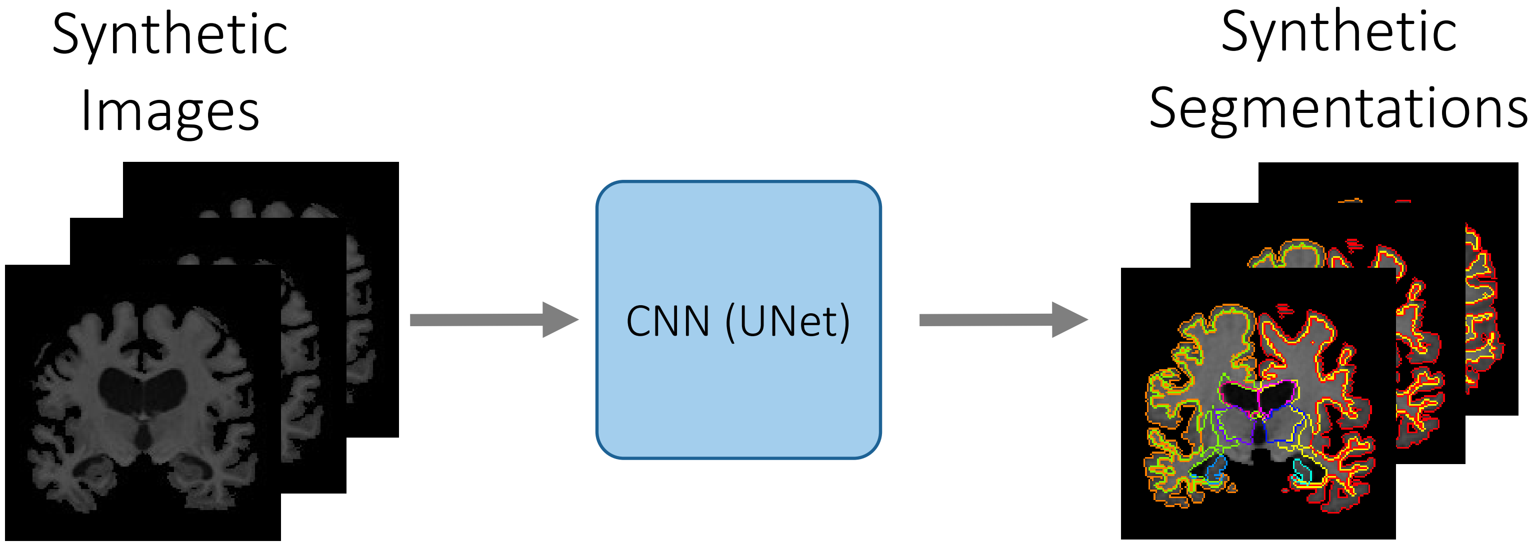
- Segmentation given a **single** segmented volume





Zhao CVPR 2019





Billot MIDL 2020

Registration usecase: segmentation

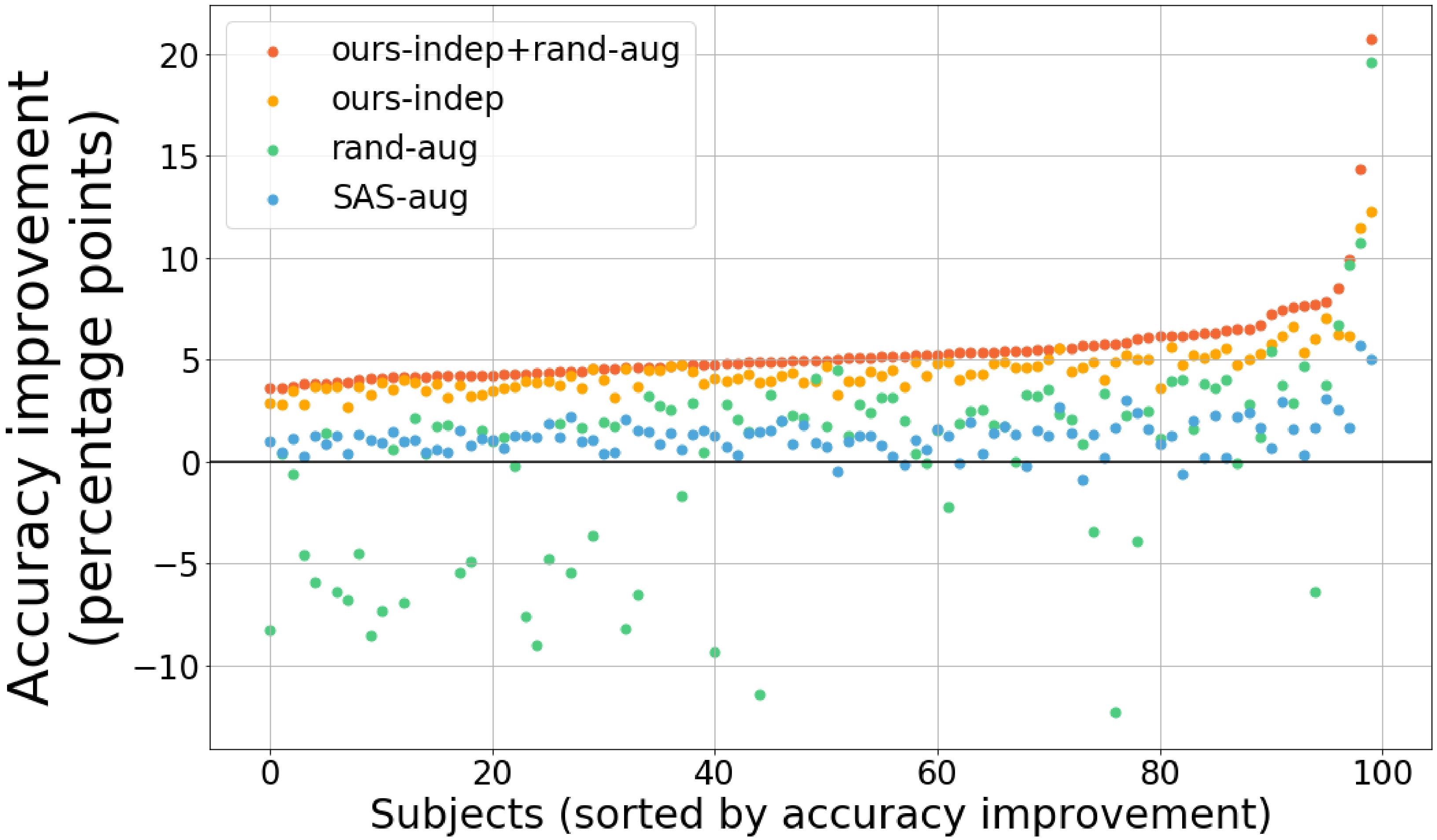
- Register segmented scan to new scan, propagate labels

- Smartly warp (image, segmentation) to creates synthetic data.
  Then use supervised segmentation

- Synthesize images *from* segmentation map
  Then use supervised segmentation

Zhao CVPR 2019
Dalca MICCAI 2019
Billot MIDL 2020

Results



Zhao et al, 2019

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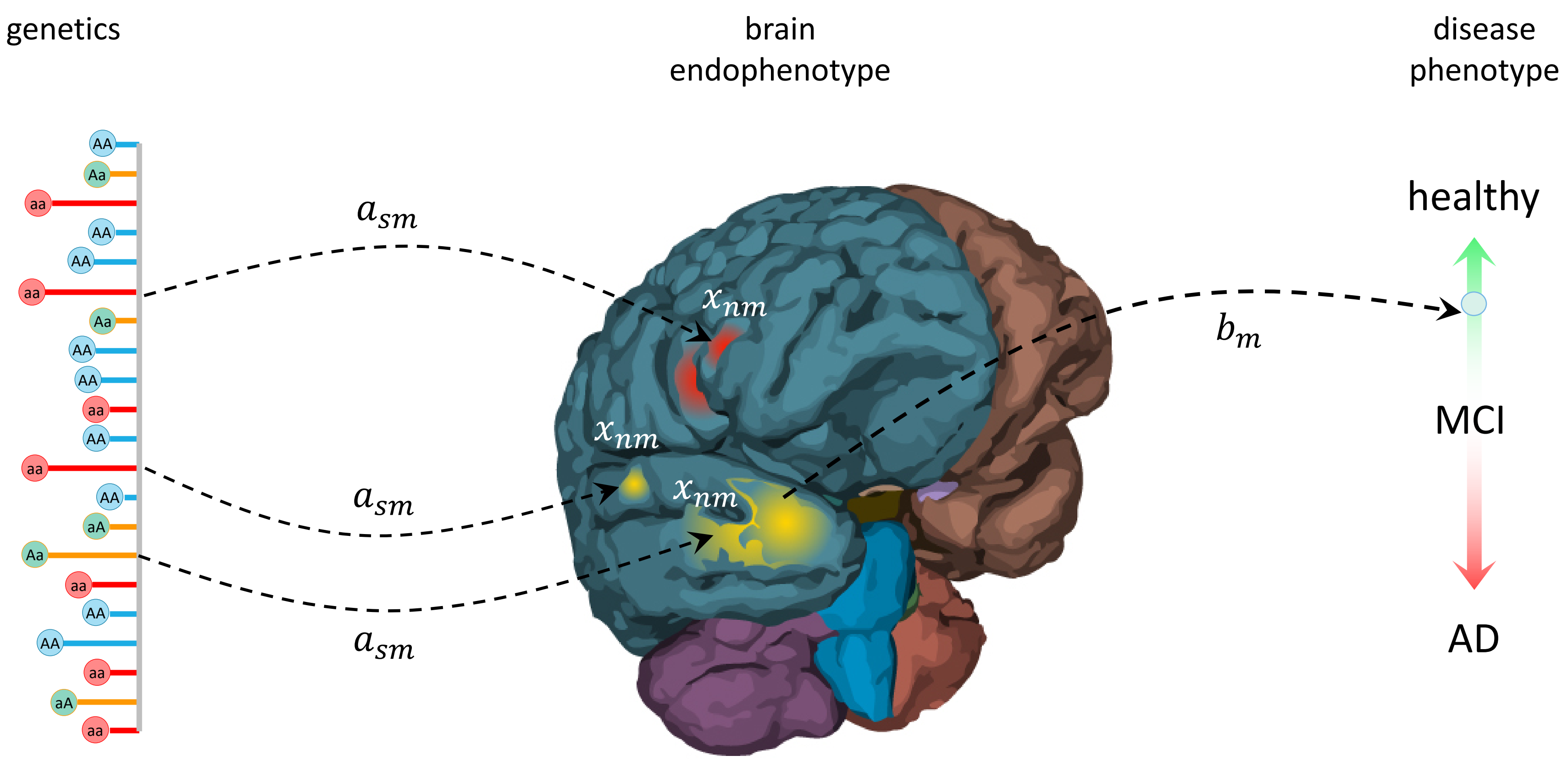
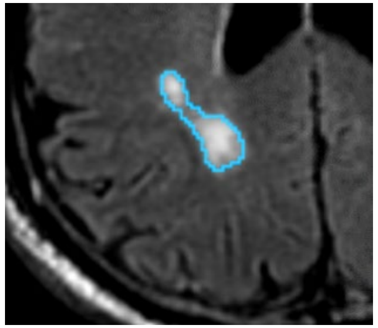

genetics
brain endophenotype
disease phenotype
AA
Aa
aa
aA
a_{sm}
a_{sm}
a_{sm}
x_{nm}
x_{nm}
x_{nm}
b_m
healthy
MCI
AD

Imaging for genetic discovery

GWAS and LMMs

$$Y = W\beta + G\gamma + \epsilon \ \ldots$$



Imaging phenotype:

- Volumes of anatomical structures or disease: **segmentation**
- Change over time (e.g. atrophy): **registration**
- **Can we learn the phenotype?**

Genetics for image (anatomical) prediction

Scan at age 50

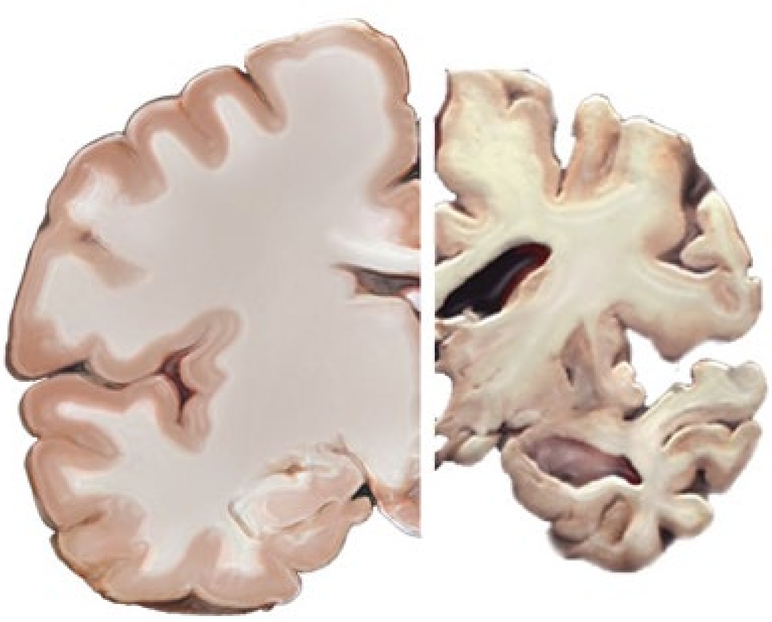
Scan at age 60

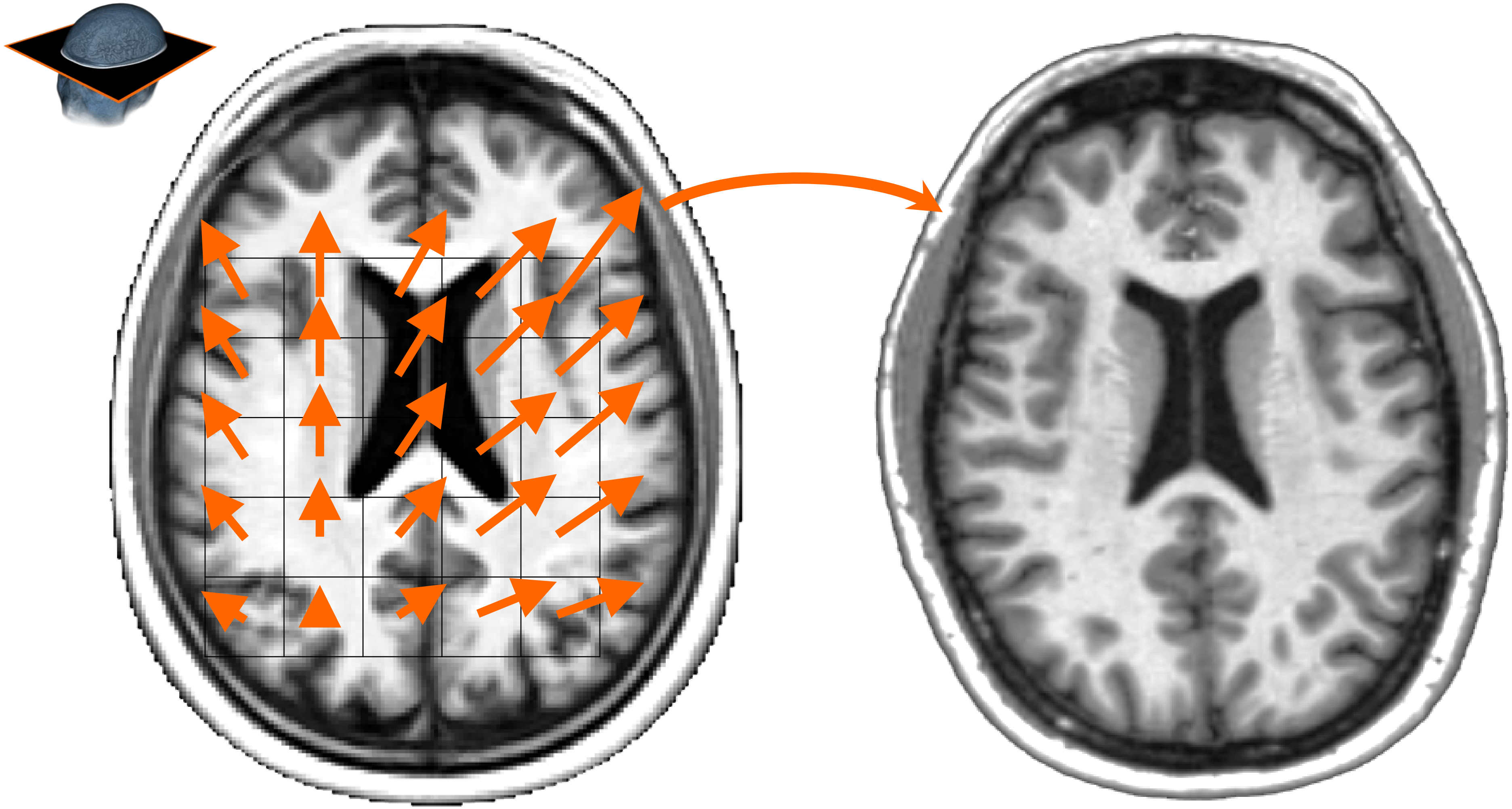
Dalca MICCAI 2015, Rakic MIDL 2020

Motivation

Healthy Brain

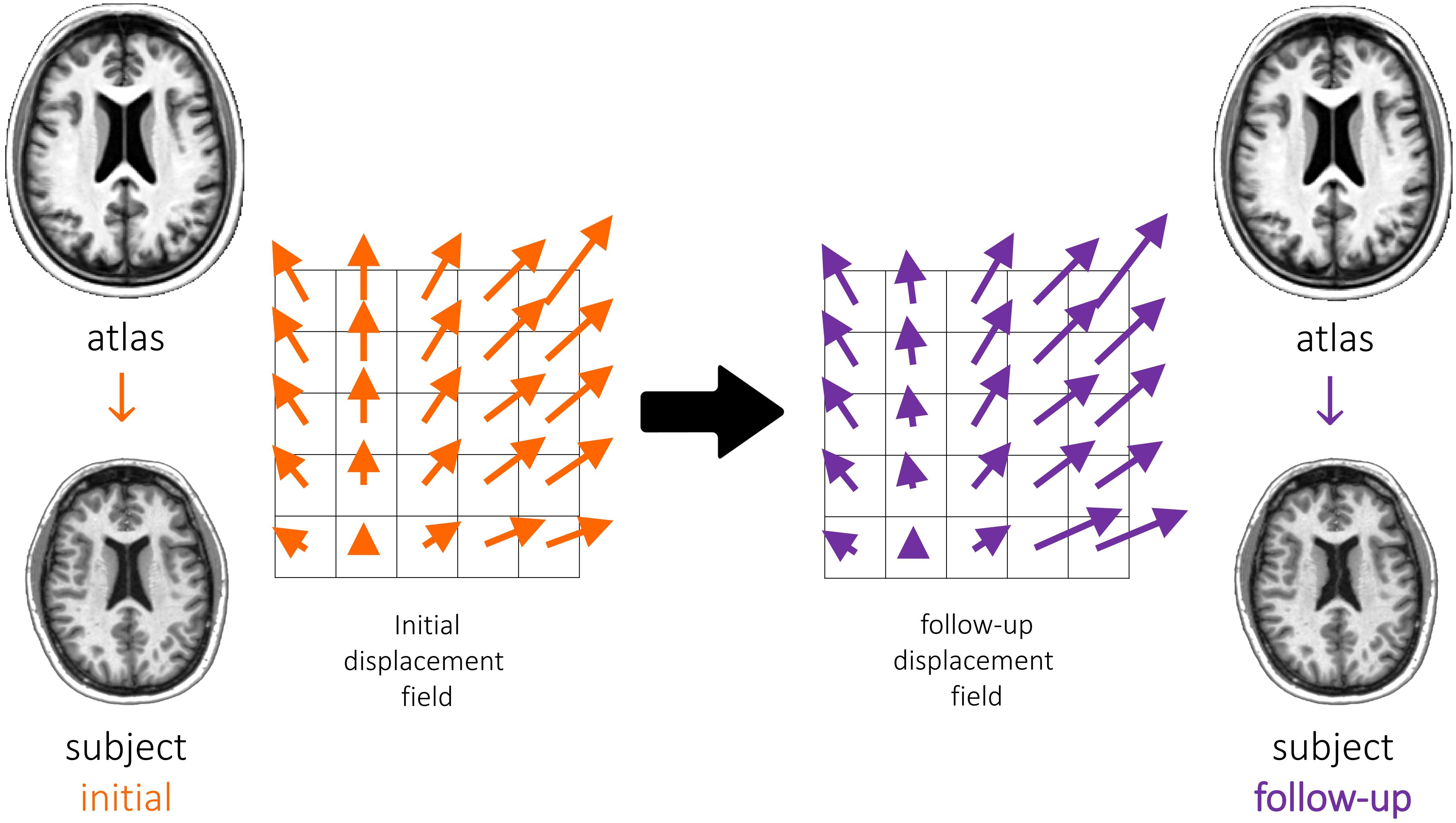
Severe Alzheimer's





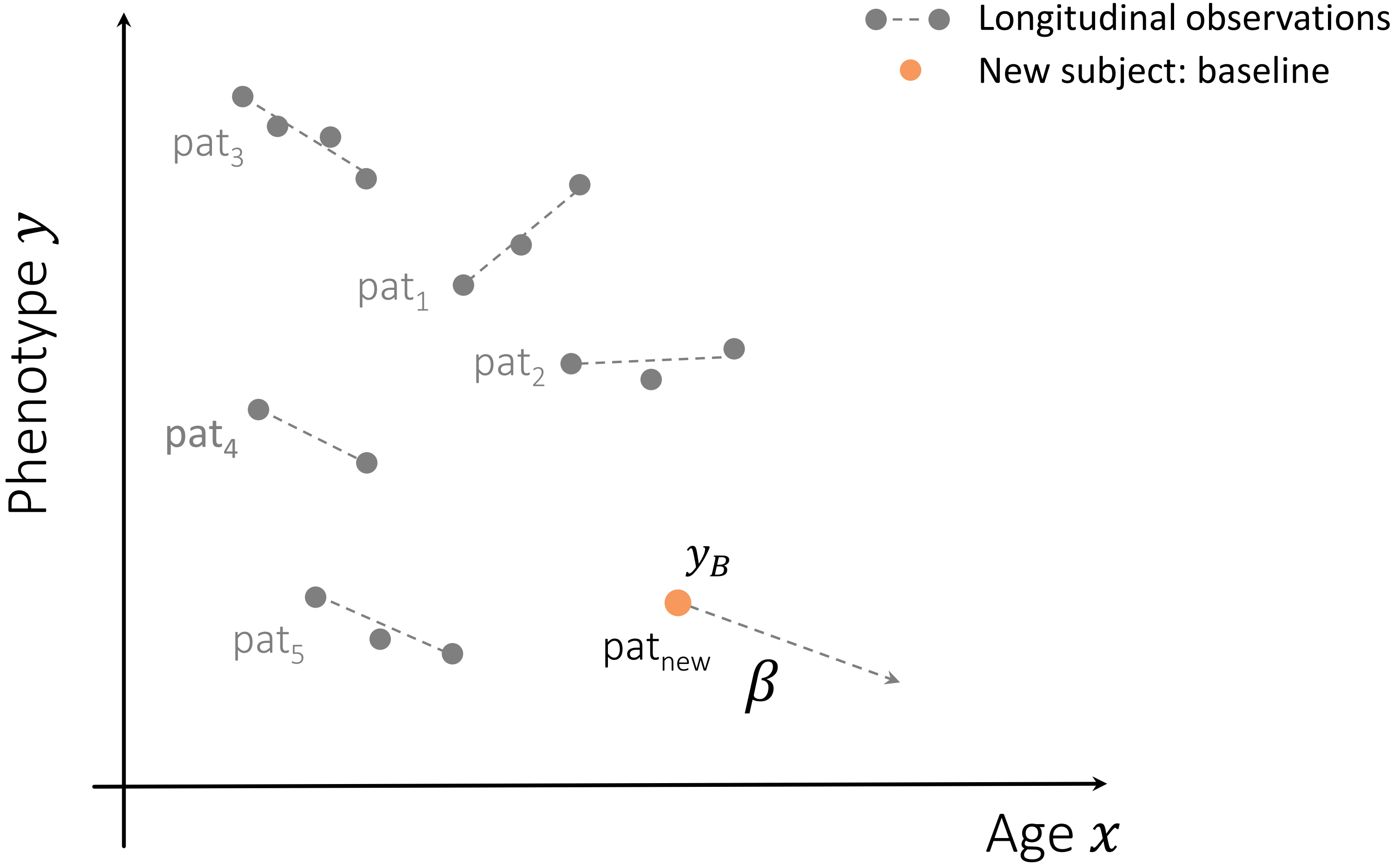
Atlas
(average brain)

Subject
medical scan

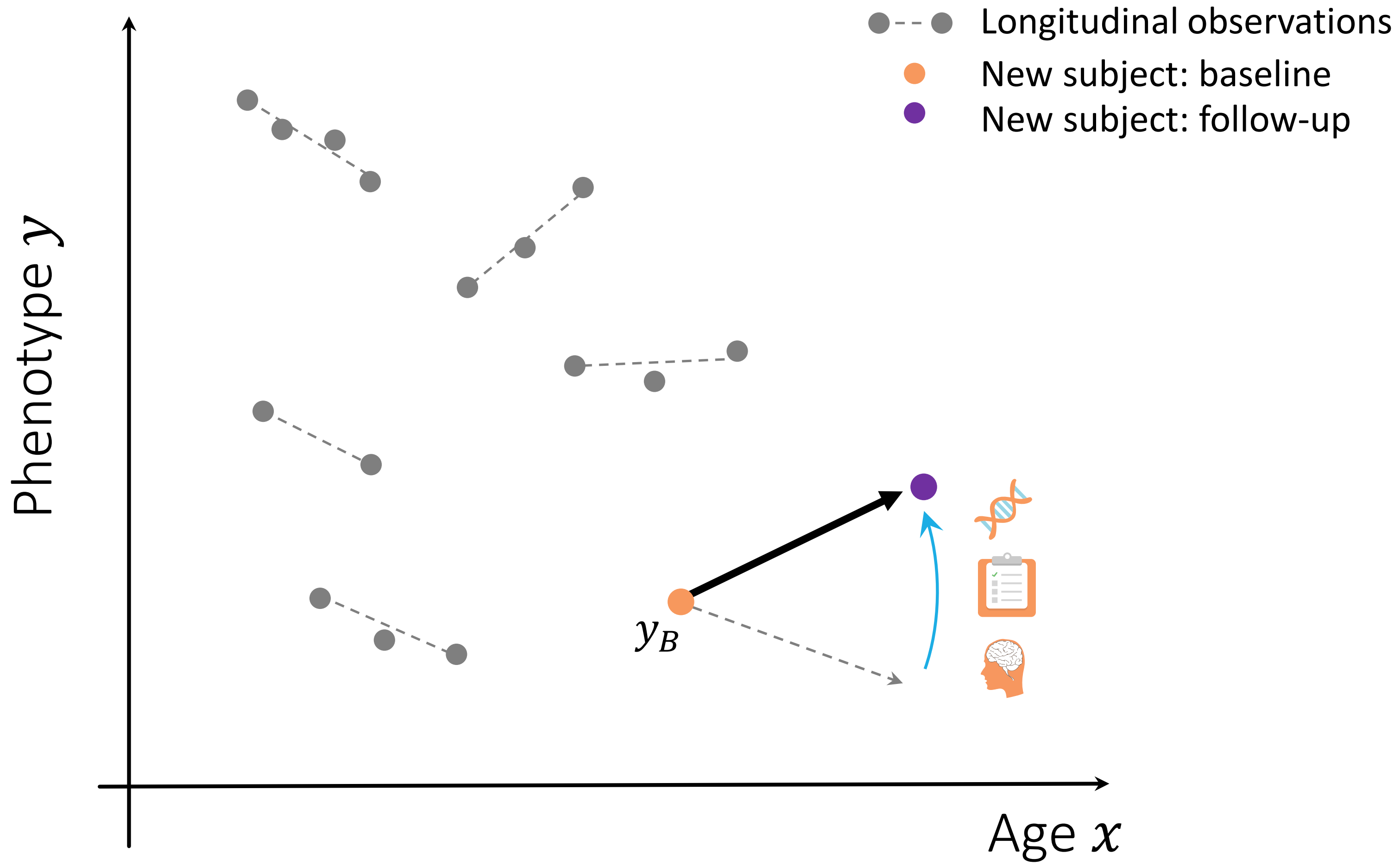

atlas
subject
initial
Initial
displacement
field
follow-up
displacement
field
atlas
subject
follow-up

Scalar Phenotype Change


Longitudinal observations
Phenotype y
pat$_1$
Age x



$$y_t = y_B + \Delta x_t \beta$$



$$y_t = y_B + \Delta x\,(\beta + h_G + h_C + h_y) + \epsilon$$

Model

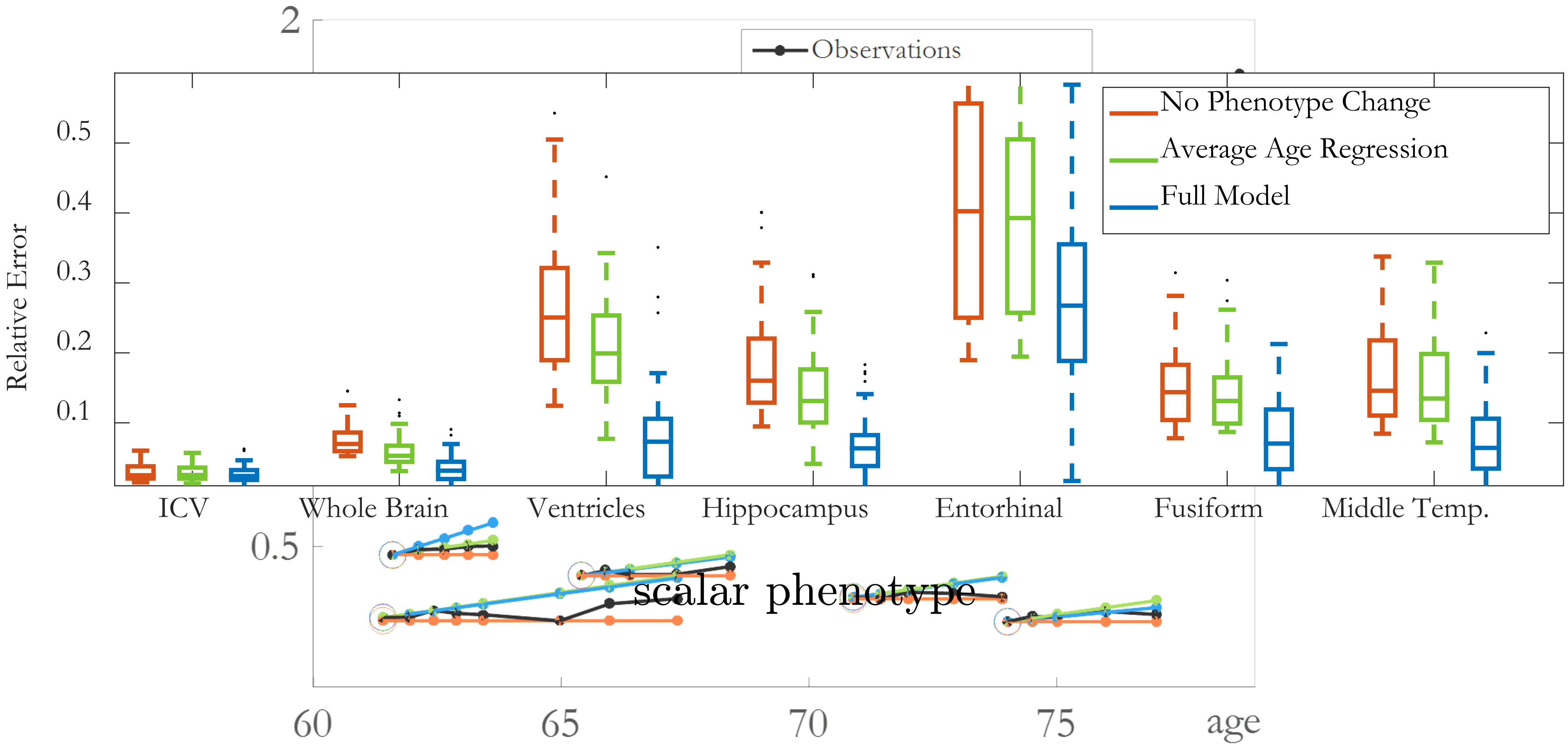
$$\boxed{y_t = y_B + \Delta x\,(\beta + h_G + h_C + h_y) + \epsilon}$$

$$h_X(z_i) \sim \sum_j \overbrace{\alpha_j}^{\text{subject } j \text{ param.}} \; \underbrace{K_X(z_i, z_j)}_{\text{phenotype } z \text{ similarity}}$$

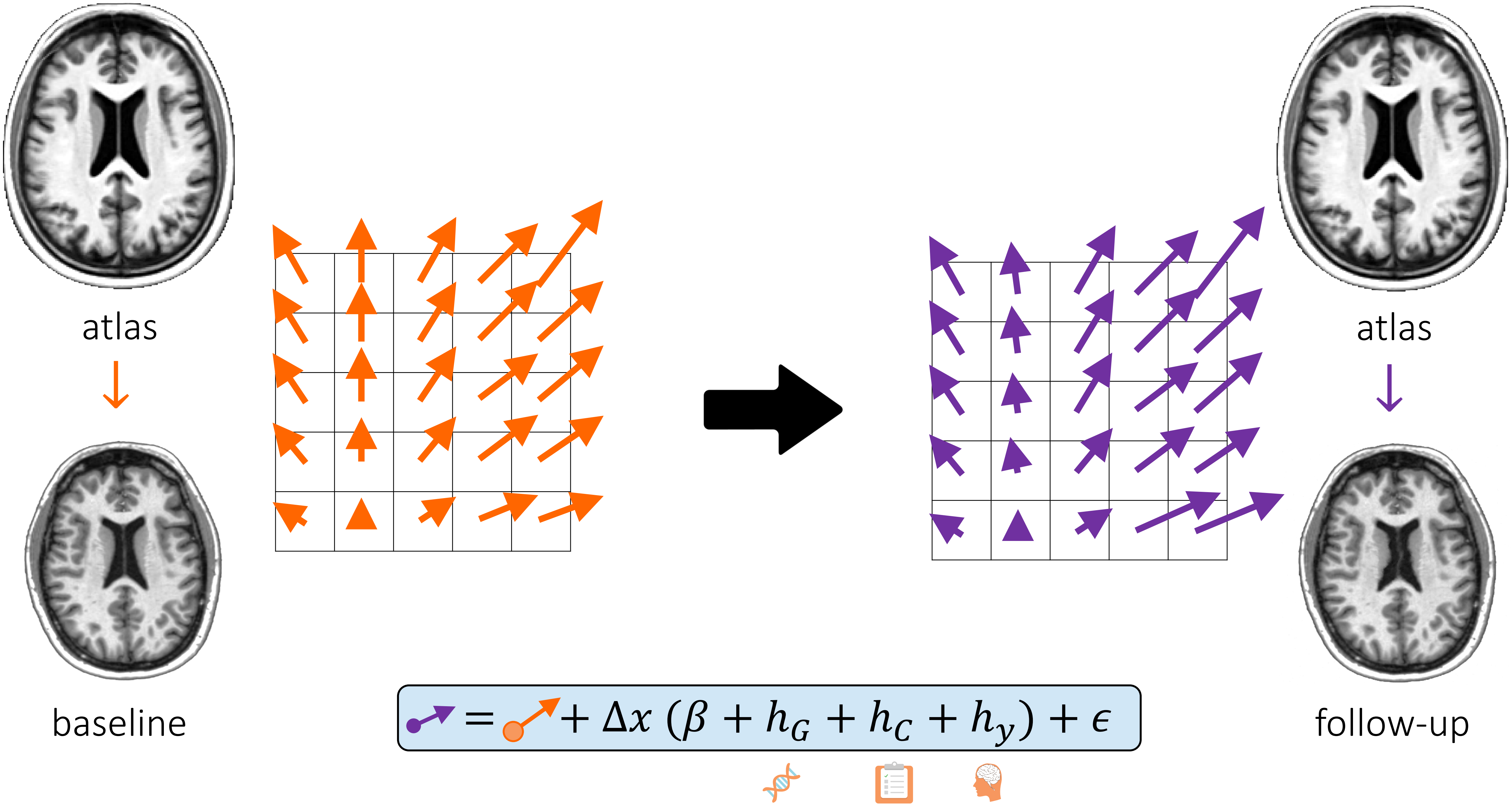
Genetics Kernel

Main parameters: α_j and β

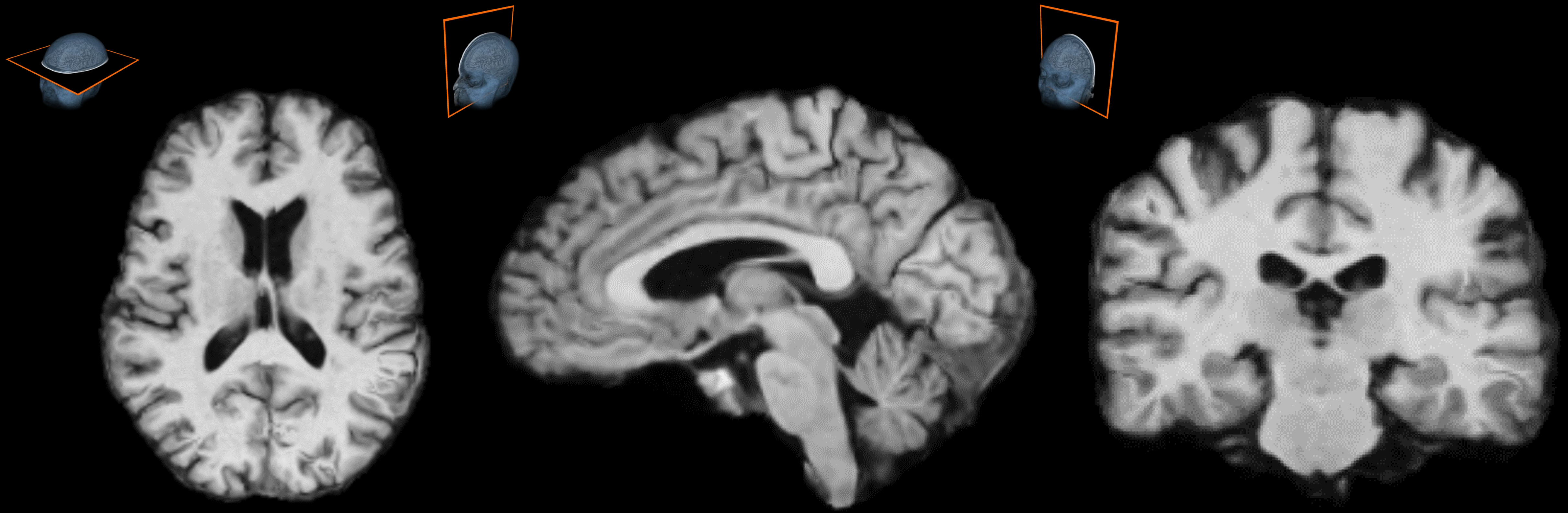
Scalar Phenotype Results



Predict Anatomical Scans

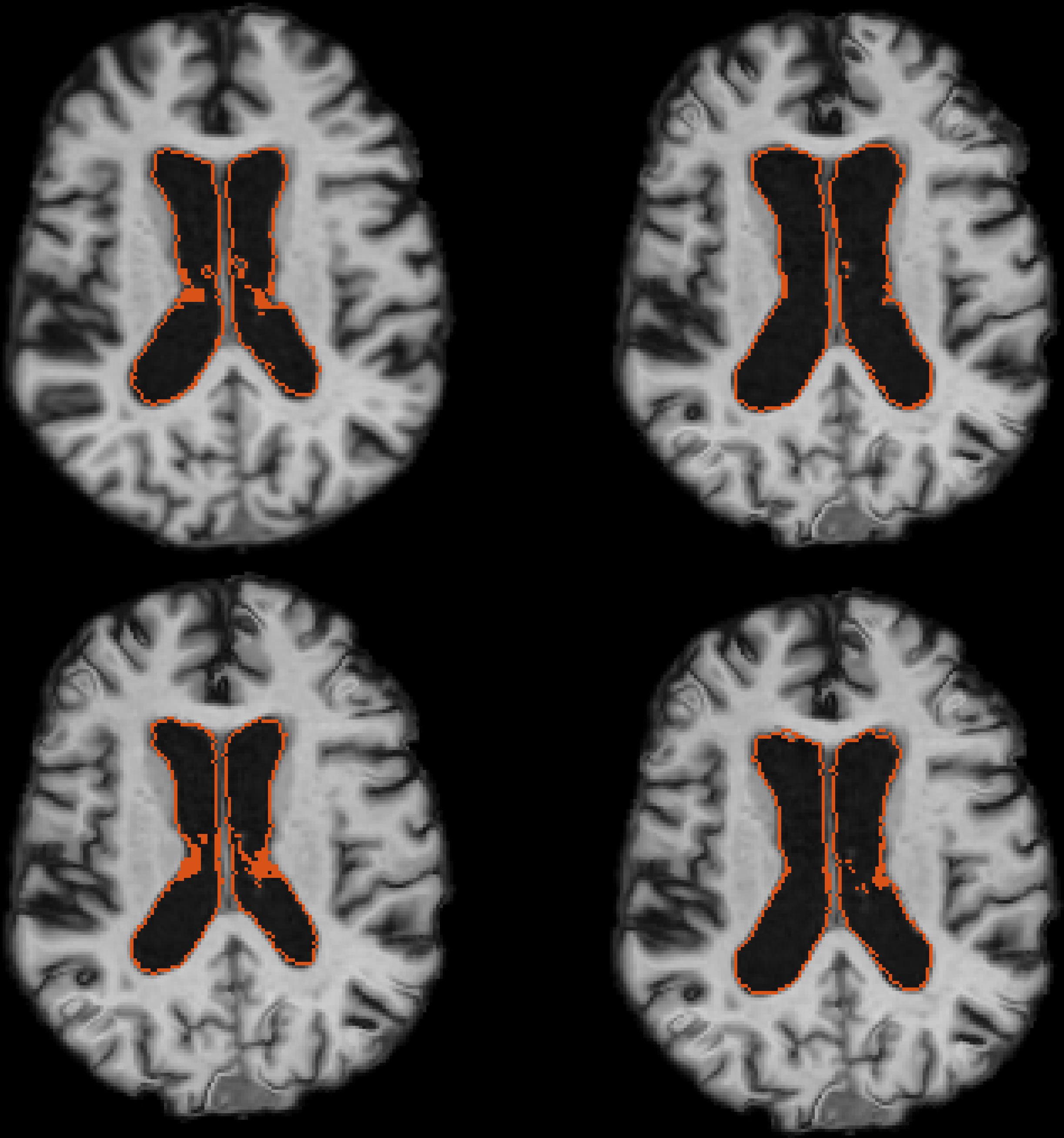

atlas
baseline
atlas
follow-up
$= + \Delta x\,(\beta + h_G + h_C + h_y) + \epsilon$

Predicted follow-up scans



Baseline

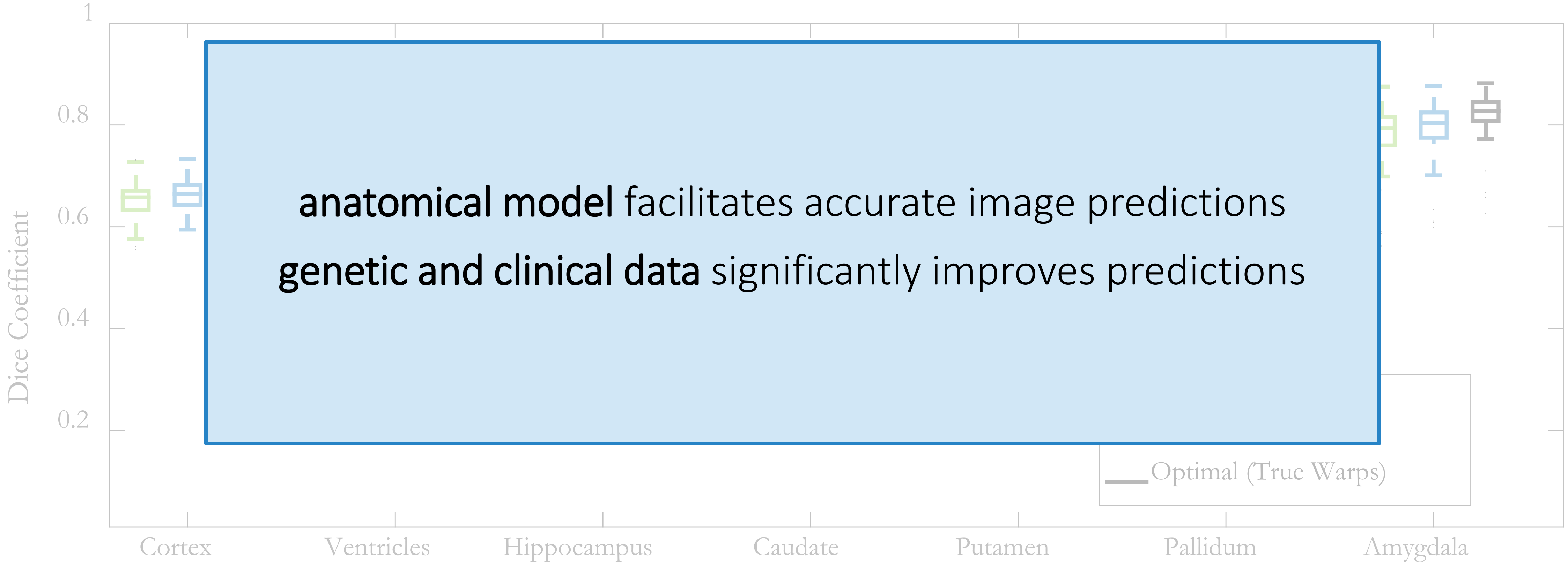
Follow-up



Average Age Regression Predicted Follow-up

Our Full Model Predicted Follow-up

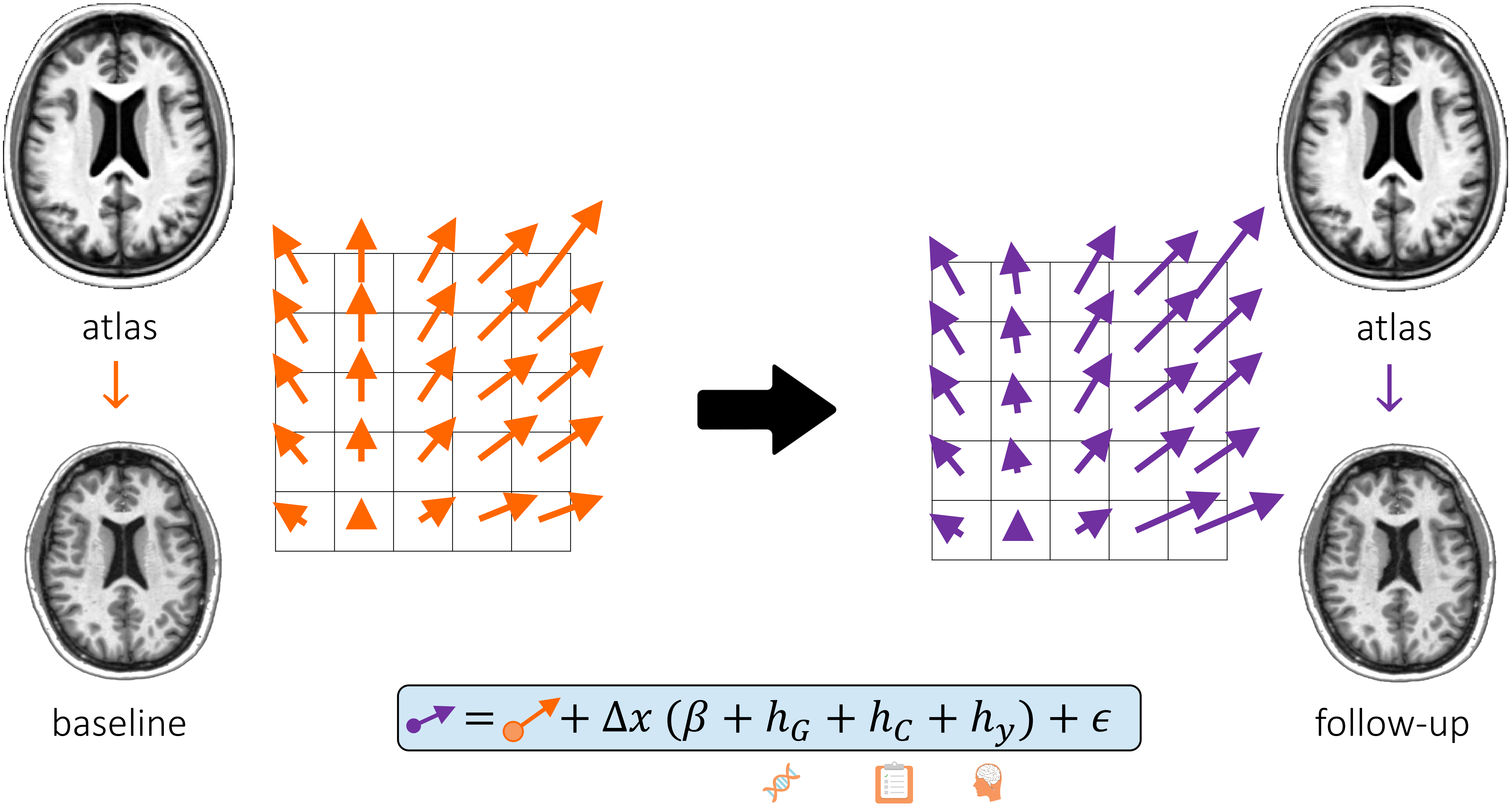
Volume overlap: predicted vs real structures

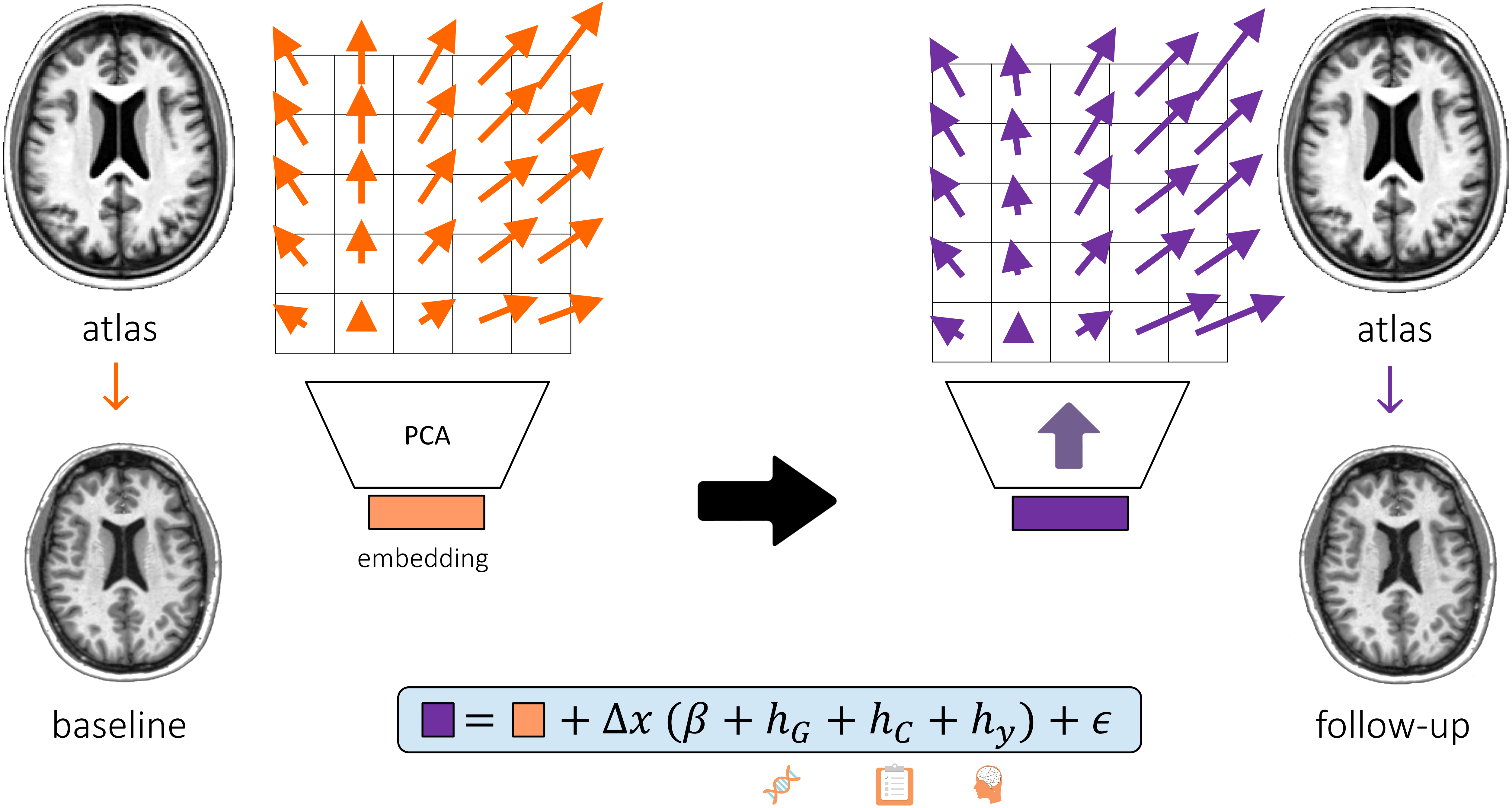


anatomical model facilitates accurate image predictions

genetic and clinical data significantly improves predictions

Questions?


atlas
baseline
atlas
follow-up
$= + \Delta x\,(\beta + h_G + h_C + h_y) + \epsilon$

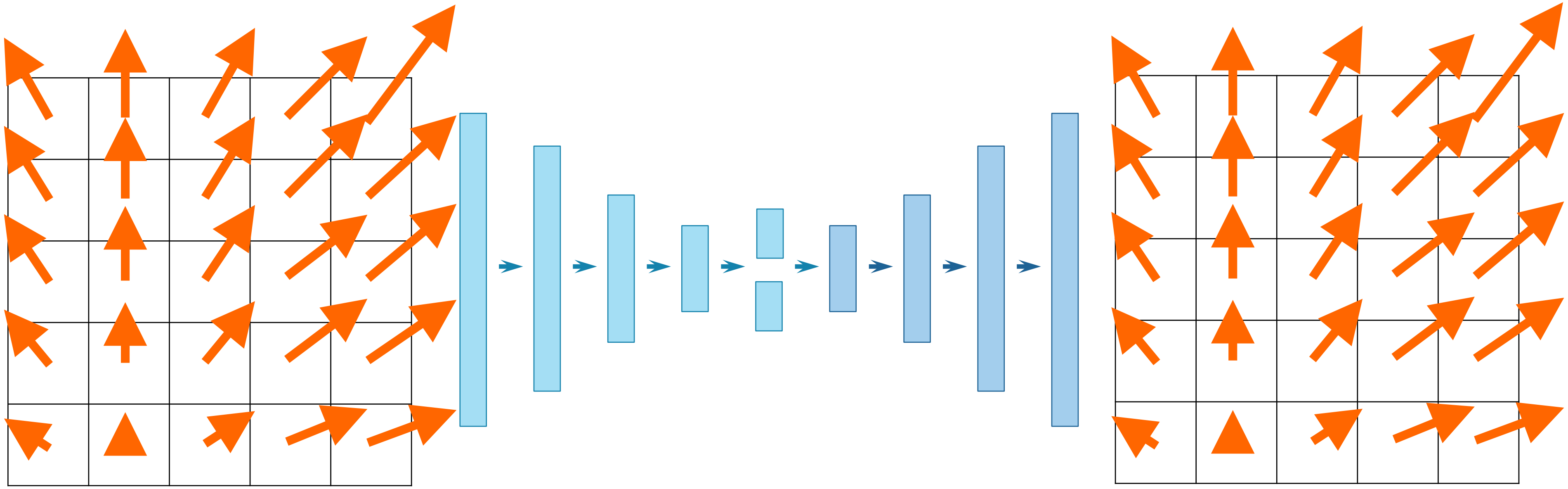

atlas
baseline
PCA
embedding
atlas
follow-up
$= + \Delta x\,(\beta + h_G + h_C + h_y) + \epsilon$

Linear models don’t capture imaging or deformations well

What to do?

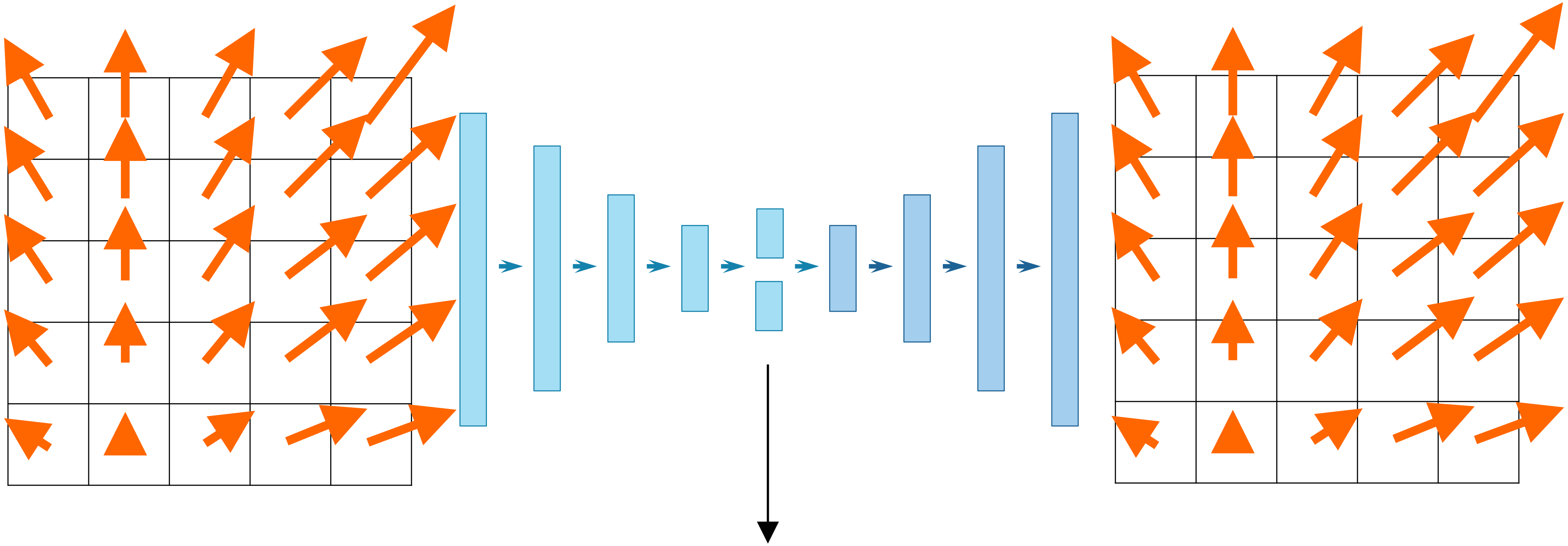
Gaussian Process Prior VAE

- Capture deformations with a VAE: $p(z)\, p(\phi|z)$



Gaussian Process Prior VAE

- Capture deformations with a VAE: $p(z)\ p(\phi|z)$
- Insert external data in the prior $p(z; G, C, y)$ using Gaussian process!



$$h_G + h_C + h_y$$

Casale NeurIPS 2018
Rakic et al, MIDL short 2020

Questions?

Outline

- Overview of Medical Imaging
  - Utility and properties
- **Example**: Segmentation
  - *Classical* and deep learning approaches
- **Example**: Registration (alignment):
  - Optimization and learning approaches
- **Example**: Imaging genetics
- Takeaways

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