Statistical Learning Methods for Neuroimaging Data Analysis

NESS 2022 Symposium Lecture 2

Image Analysis Methods

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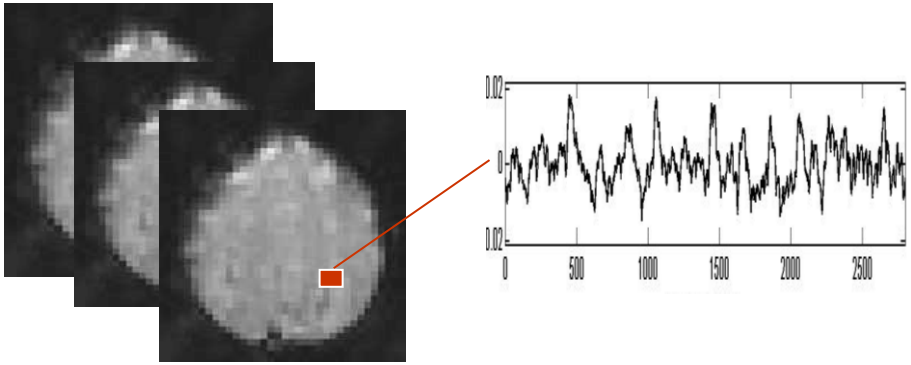
Reading Materials

1. Bankman, I. (Ed.). (2008). *Handbook of medical image processing and analysis*. Elsevier.
2. Bauer, Stefan, Roland Wiest, Lutz-P. Nolte, and Mauricio Reyes. "A survey of MRI-based medical image analysis for brain tumor studies." *Physics in Medicine & Biology* 58, no. 13 (2013): R97.
3. Fu, Yabo, Yang Lei, Tonghe Wang, Walter J. Curran, Tian Liu, and Xiaofeng Yang. "Deep learning in medical image registration: a review." *Physics in Medicine & Biology* 65, no. 20 (2020): 20TR01.
4. Litjens, Geert, Thijs Kooi, Babak Ehteshami Bejnordi, Arnaud Arindra Adiyoso Setio, Francesco Ciompi, Mohsen Ghafoorian, Jeroen Awm Van Der Laak, Bram Van Ginneken, and Clara I. Sánchez. "A survey on deep learning in medical image analysis." *Medical image analysis* 42 (2017): 60-88.
5. Modersitzki, Jan. *FAIR: flexible algorithms for image registration*. Society for Industrial and Applied Mathematics, 2009.
5. Pham, Dzung L., Chenyang Xu, and Jerry L. Prince. "Current methods in medical image segmentation." *Annual review of biomedical engineering* 2, no. 1 (2000): 315-337.
6. Shen, Dinggang, Guorong Wu, and Heung-Il Suk. "Deep learning in medical image analysis." *Annual review of biomedical engineering* 19 (2017): 221-248.
7. Marron, James Stephen, and Ian L. Dryden. *Object Oriented Data Analysis*. Chapman and Hall/CRC, 2021.

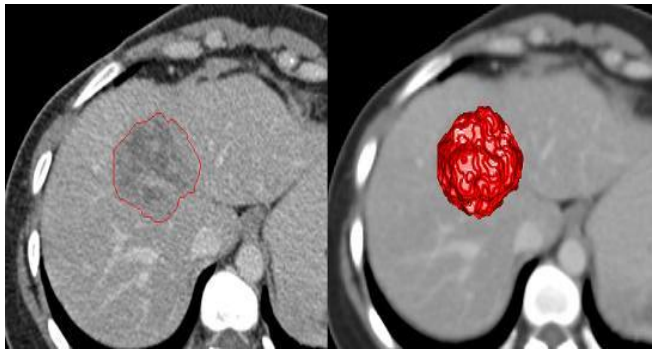
Part 1. Overview: Image Analysis

Individual Image Analysis

Reconstruction



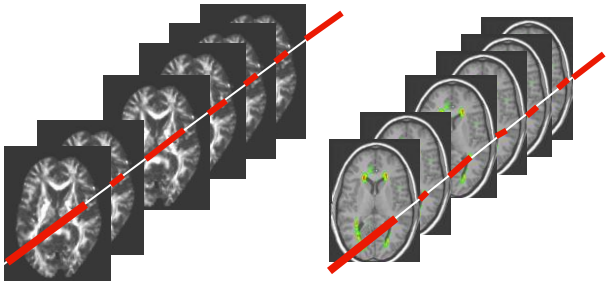
Segmentation



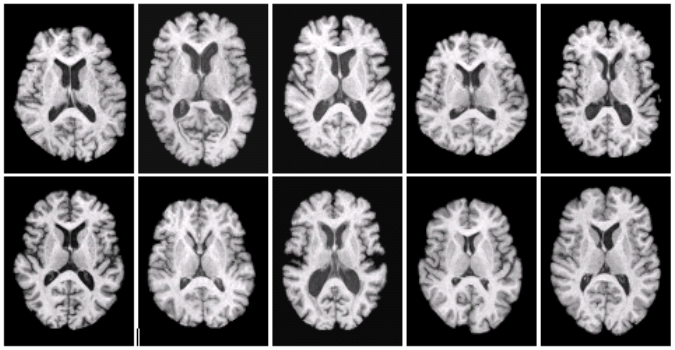
Multimode analysis

DTI

FLAIR

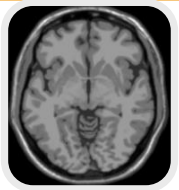


Registration

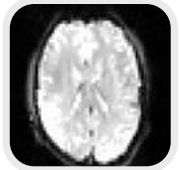


Marc

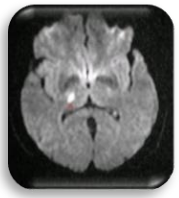
Medical Image Analysis



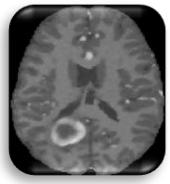
sMRI



fMRI

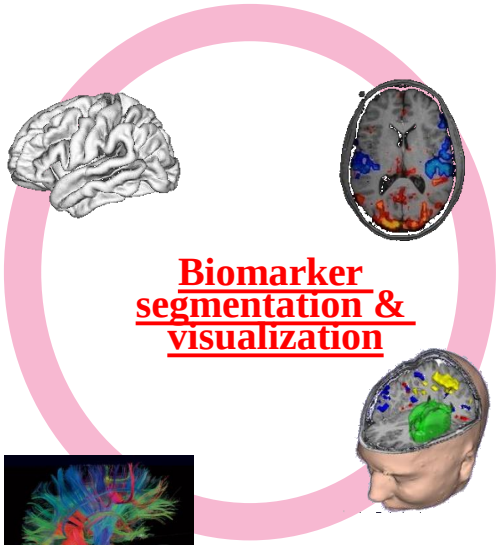


DTI



Tumor image

Image Analysis



Diagnosis

Detection

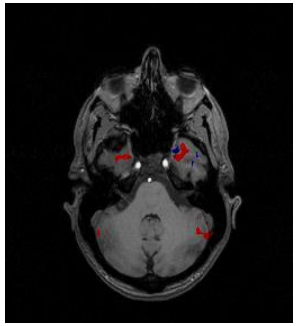
Diagnosis

Surgery Planning

Prognosis

Data → Knowledge

Image Processing



Raw Images

- Image Reconstruction
- Image Segmentation
- Image Registration
- Image Smoothing

→ Multiple Comparisons

→ Statistical Modelling

Image Processing

Image Acquisition

Signal Models & Noise Sources

Image Preprocessing

Mathematics & Statistics & Machine Learning

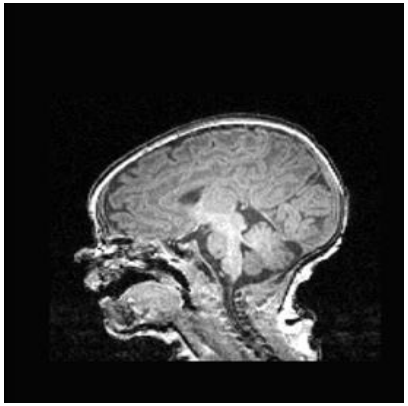
Representation Segmentation Registration

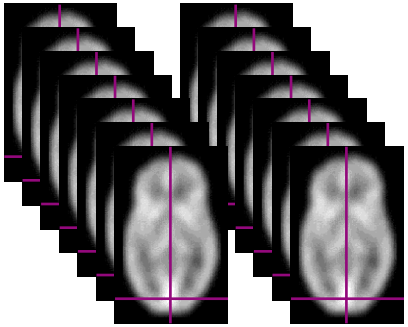
Data Analysis & Interpretation

Statistical Modeling & Inference

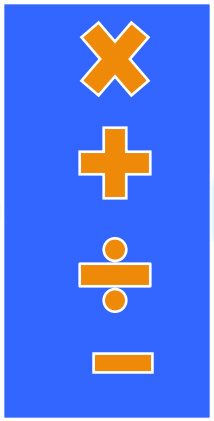
Image Processing

$$f$$

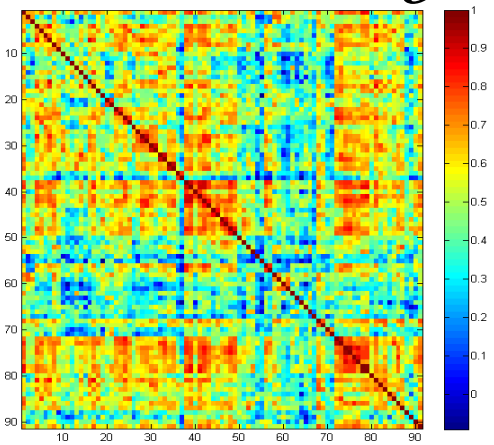


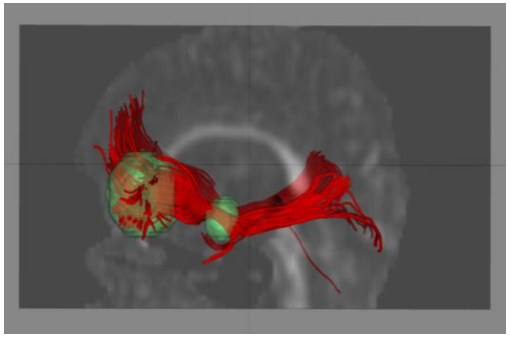


$$T$$

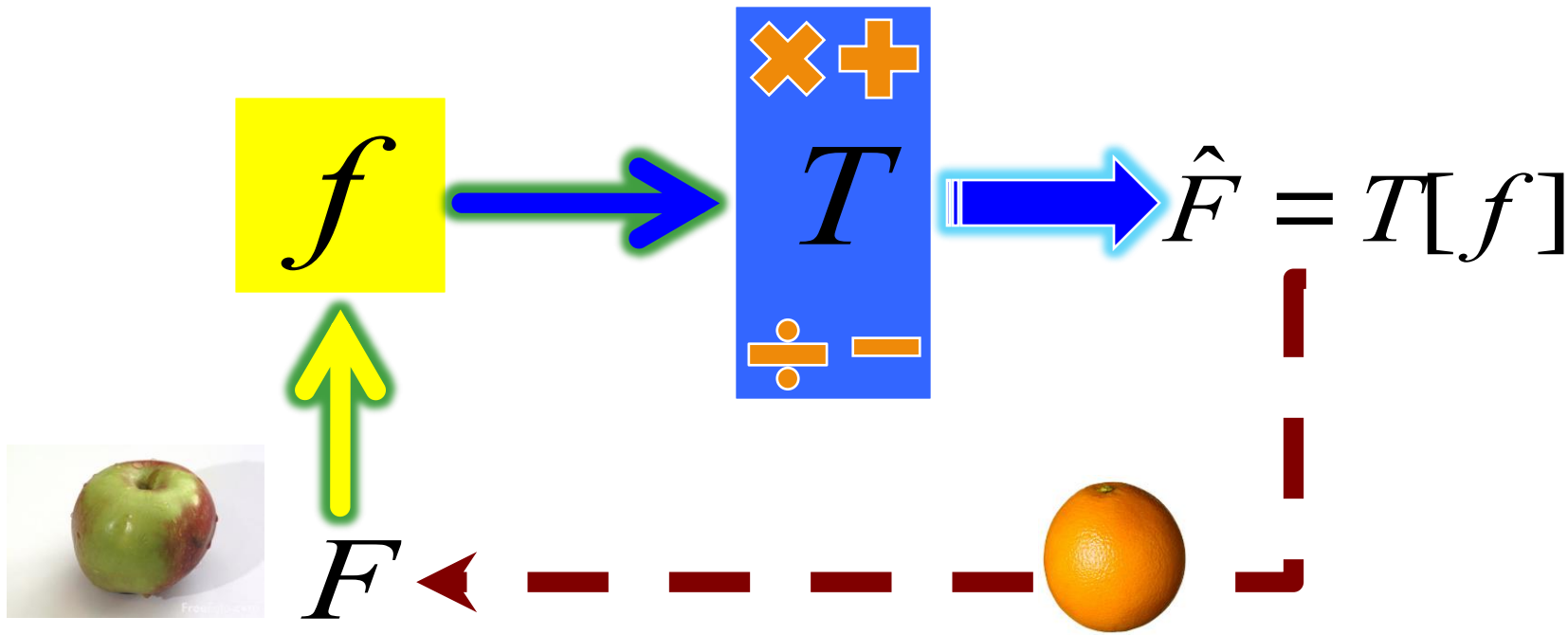


$$\hat{F} = T[f]$$





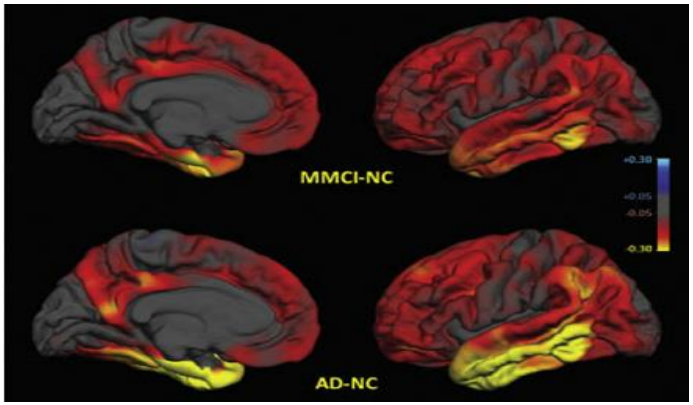
ill-posed inverse problems



$$d(F, \hat{F}) \to 0?$$

Population Image Analysis

Group Analysis



Prediction

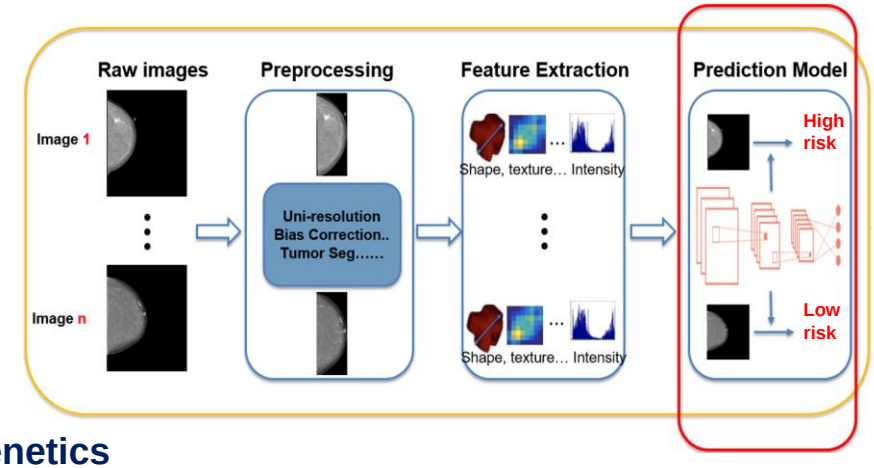
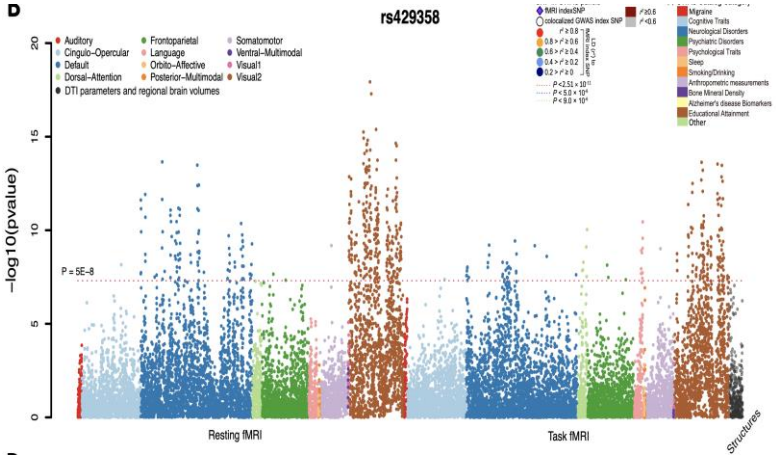
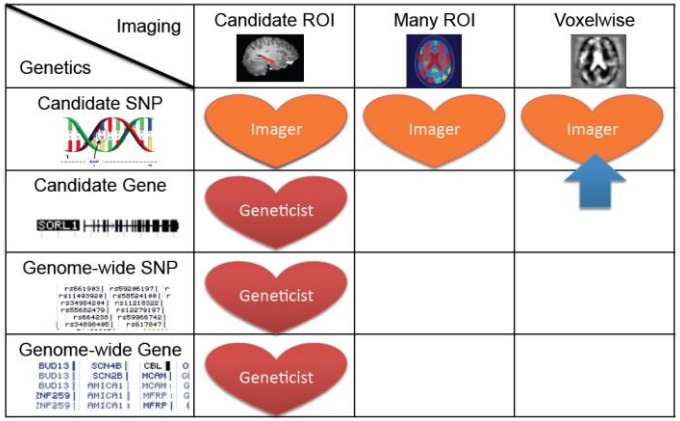


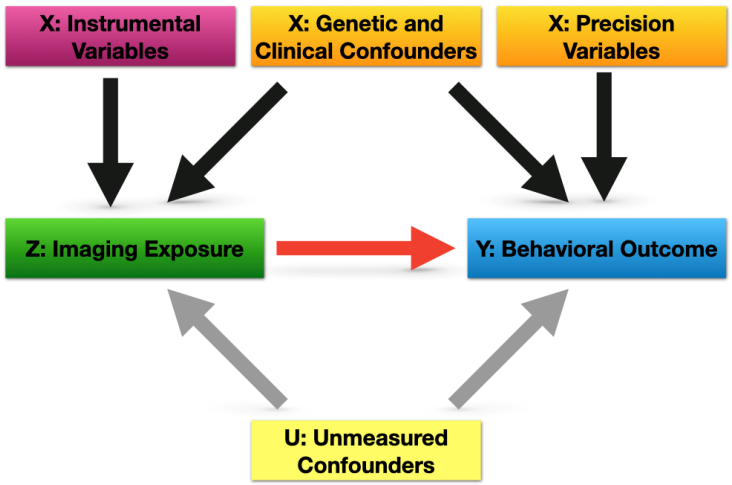
Image Genetics



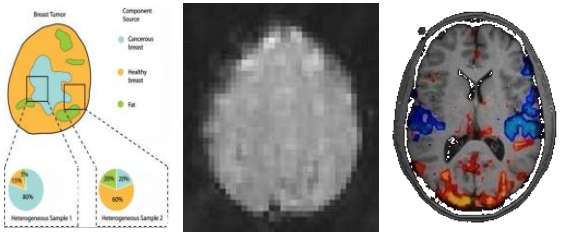


Population Image Analysis

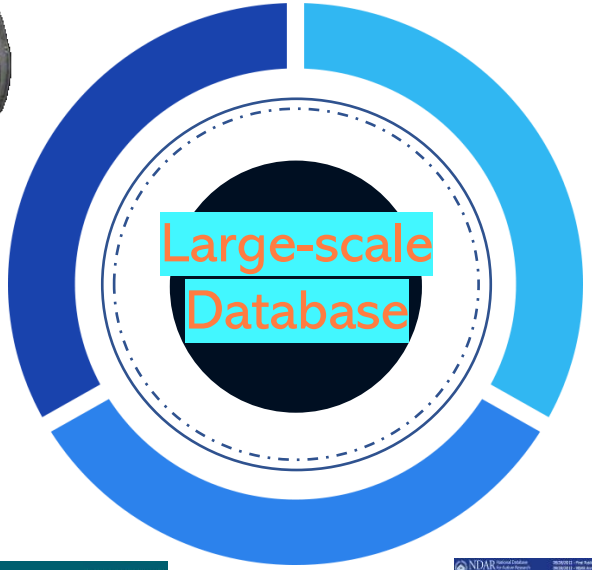
- Causal and mediation inference
- Experiment design
- Data integration
- Dimensional reduction methods
- Imaging genetics
- Imputation methods
- Knowledge-based system
- Object oriented data analysis
- Predictive models
- Statistical parametric mapping

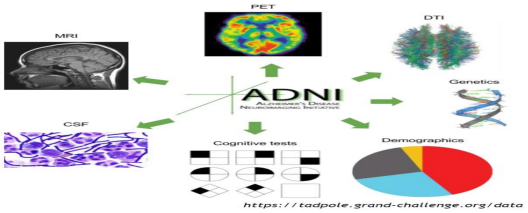


Ecological Layout

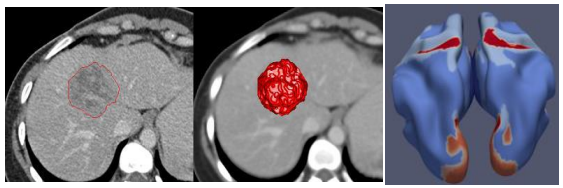


Deconvolution

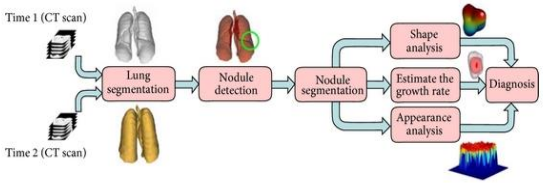




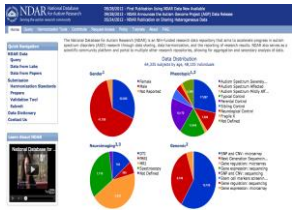
Integration



Learning



Prediction



Part 2. Individual Image Analysis

Digital Imaging and Communications in Medicine

DICOM is a standard for handling, storing, printing, and transmitting information in medical imaging.

- **It includes a file format definition and a network communications protocol.**
- **The communication protocol is an application protocol that uses TCP/IP (Transmission Control Protocol/Internet Protocol) to communicate between systems.**
- **DICOM files can be exchanged between two entities that are capable of receiving image and patient data in DICOM format.**
- **DICOM enables the integration of scanners, servers, workstations, printers, and network hardware from multiple manufacturers into a picture archiving and communication system (PACS).**
- **The different devices come with DICOM conformance statements which clearly state the DICOM classes they support.**

Analyze

Analyze 7.5 is a 3-D biomedical image visualization and analysis product developed by the Biomedical Imaging Resource of the Mayo Clinic.

- An Analyze 7.5 data set is made of two files, a header file and an image file.
- The files have the same name with different file extensions.
- The header file has the file extension .hdr and the image file has the file extension .img.
- info = analyze75info(filename,'ByteOrder', *endian)*

reads the Analyze 7.5 header file using the byte ordering specified by endian, where endian can have either of the following values:

'ieee-le' Byte ordering is Little Endian;

'ieee-be' Byte ordering is Big Endian.

- Read image data from image file of Analyze 7.5 data set

X = analyze75read(filename) X = analyze75read(info)

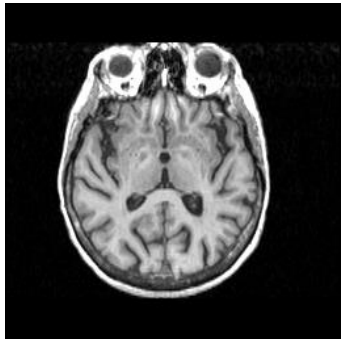
NIfTI

NIfTI-1 is adapted from the widely used ANALYZE™ 7.5 file format. NIfTI-1 uses the "empty space" in the ANALYZE 7.5 header to add several new features.

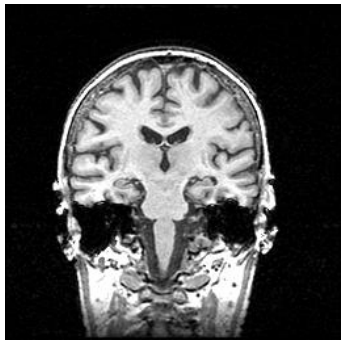
These new features include

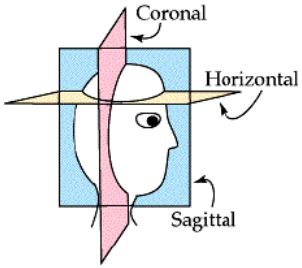
- **Affine coordinate definitions relating voxel index (i,j,k) to spatial location (x,y,z);**
- **Codes to indicate spatio-temporal slice ordering for FMRI;**
- **"Complete" set of 8-128 bit data types;**
- **Standardized way to store vector-valued datasets over 1-4 dimensional domains;**
- **Codes to indicate data "meaning";**
- **A standardized way to add "extension" data to the header;**
- **Dual file (.hdr & .img) or single file (.nii) storage.**

Orientation

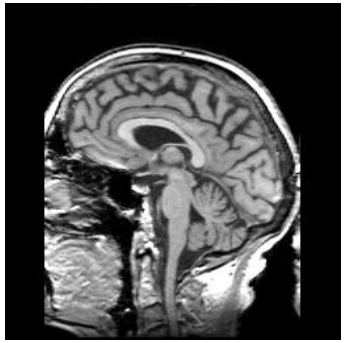


Axial
(trans-axial,
horizontal)

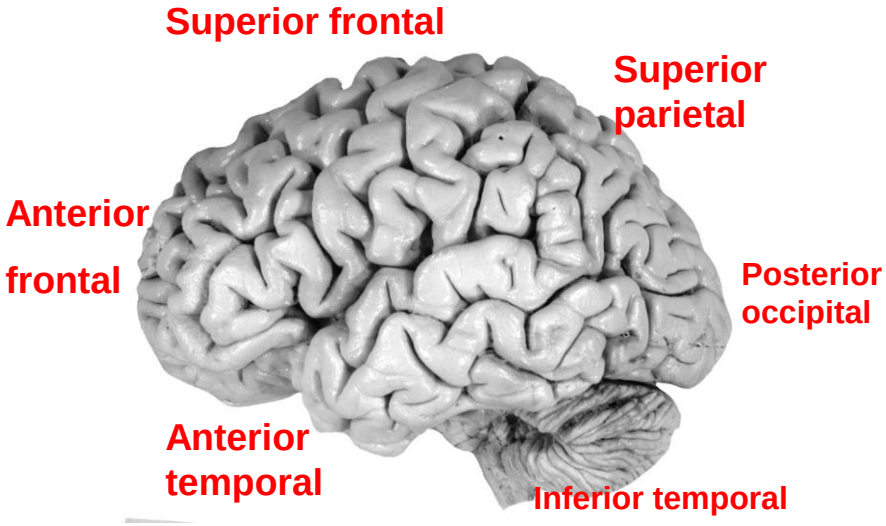




Coronal



Sagittal



RAS versus LAS

The default ANALYZE orientation is LAS (radiological orientation)

+X is Left
+Y is Anterior
+Z is Superior

for LAS (radiological convention) image, right cerebral hemisphere is at LEFT and left cerebral hemisphere is at RIGHT

The neurological convention is RAS (only the direction of X is swapped)

+X is Right
+Y is Anterior
+Z is Superior

for RAS (neurological convention) image, left cerebral hemisphere is at LEFT and right cerebral hemisphere is at RIGHT;

UseANALYZE.pdf

Input File Format ANALYZE

Output File Format NifTI

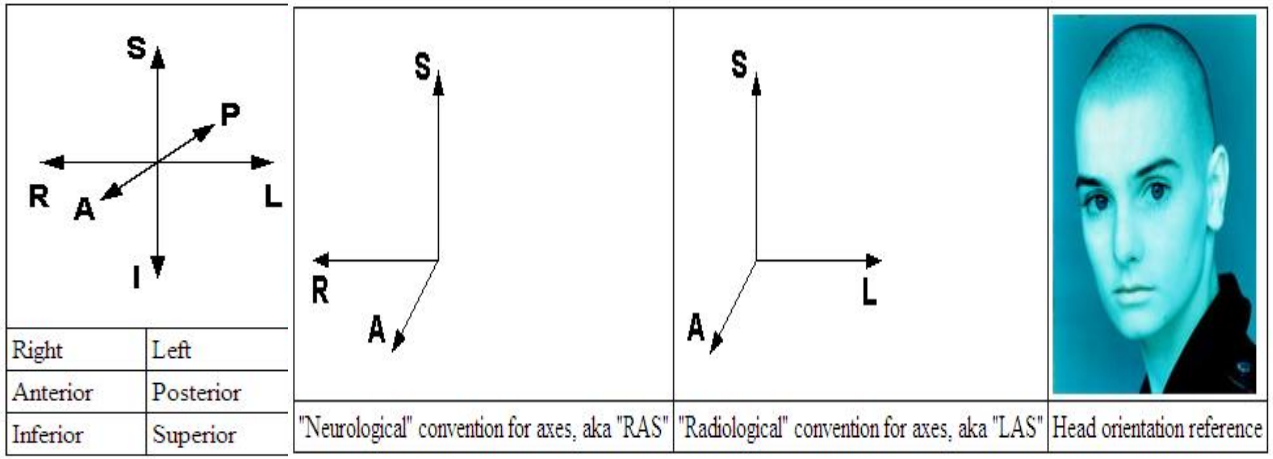


Image Inpainting

is an artistic synonym for image interpolation. Given some values at some points, determine continuous range of values.

From Discrete Images to Continuous Images

- Uses:
  - Synthesis
    - Morph between two images
    - Interpolate a curve between points
  - Continuous range of values between vertices.
  - Blowing up an image.

Image Interpolation

The objective is to find a function

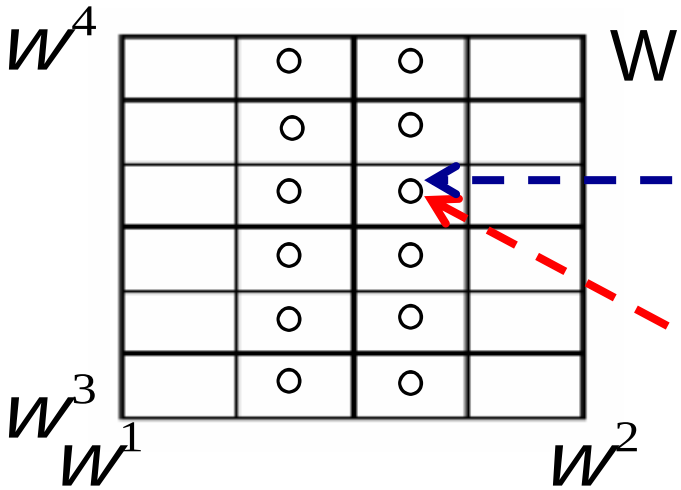
$$\mathfrak{I}(x) = \text{inter}(\mathrm{T}, \mathrm{W}, \mathrm{xc})$$

$\mathrm{T}(\cdot) = \mathrm{T}_q(\cdot)$ is the interpolation model

$\Omega = [\omega^1, \omega^2] \times \cdots \times [\omega^{2d-1}, \omega^{2d}].$

$\mathrm{xc} = [x_j = (x_j^1, \cdots, x_j^d)]_{j=1}^n$ is a collection of n points.

$$\mathfrak{I}(x_j) = \mathrm{DataT}(x_j) \quad \text{for} \quad j = 1, \cdots, n$$



$\mathrm{W} = [w^1, w^2] \times [w^3, w^4]$

$\mathrm{DataT}(x_j)$

$x_j = (x_j^1, x_j^2)$

cell-centered grids

Different Standard Interpolation Methods

- **Nearest-neighbor (proximal) interpolation is to** select the value of the nearest point, and does not consider the values of other neighboring points at all, yielding a piecewise-constant interpolant.
- **Bilinear interpolation** determines the grey level value from the weighted average of the four closest pixels to the specified input coordinates.
- **Bicubic interpolation** determines the grey level value from the weighted average of the 16 closest pixels to the specified input coordinates.

$$Q_1 = (x_1, f(x_1)), \cdots, Q_n = (x_n, f(x_n))$$

$$g(x) = \sum_{k=1}^{n} w_k U(|x - x_k|) \qquad g(x_i) = f(x_i)$$

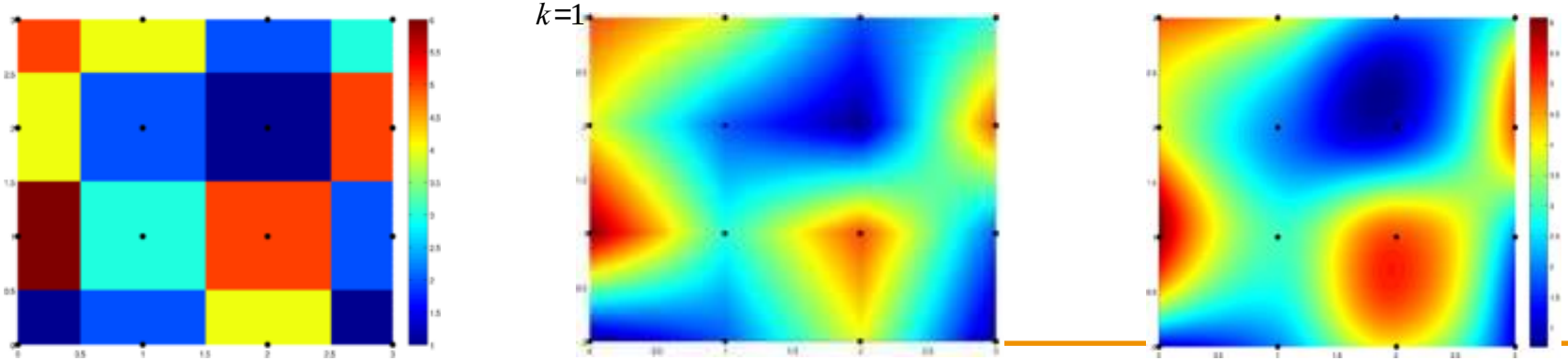
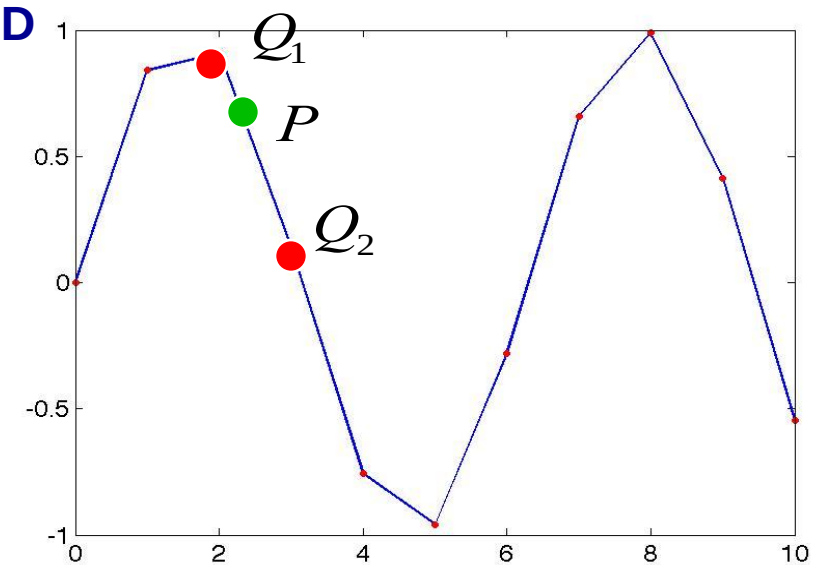
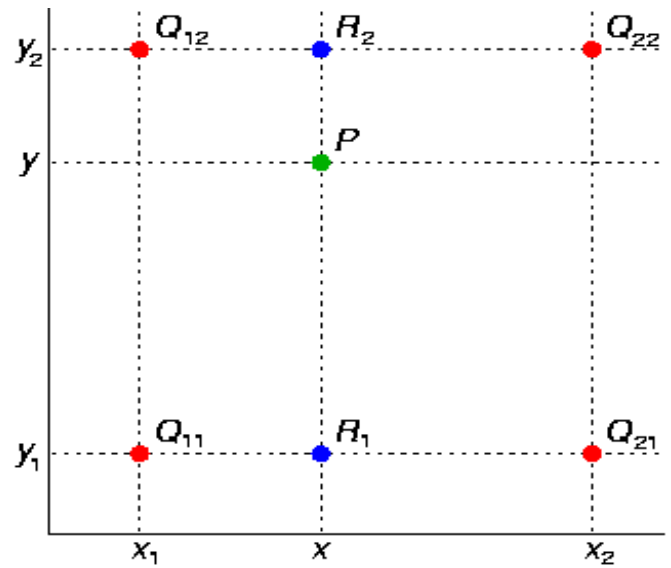


Image Inpainting

1D



2D



$$Q_1 = (x_1, f(x_1))$$

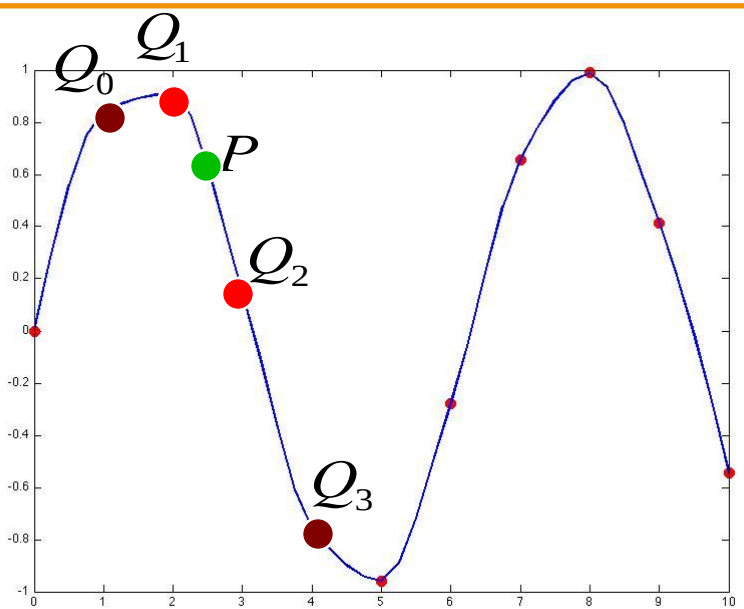
$$Q_2 = (x_2, f(x_2))$$

$$P = (x, g(x))$$

$$g(x) = f(x_1)(x - x_1)/(x_2 - x_1) + f(x_2)(x_2 - x)/(x_2 - x_1)$$

Image Inpainting

1D



	expanded	factorized	Bernstein
$h_{00}(t)$	$2t^3 - 3t^2 + 1$	$(1 + 2t)(1 - t)^2$	$B_0(t) + B_1(t)$
$h_{10}(t)$	$t^3 - 2t^2 + t$	$t(1 - t)^2$	$B_1(t)/3$
$h_{01}(t)$	$-2t^3 + 3t^2$	$t^2(3 - 2t)$	$B_3(t) + B_2(t)$
$h_{11}(t)$	$t^3 - t^2$	$t^2(t - 1)$	$-B_2(t)/3$

$$B_k(t) = \binom{3}{k} t^k (1-t)^{3-k}$$

Finite difference

$$\dot{f}(x_1) \approx \frac{f(x_2) - f(x_1)}{2(x_2 - x_1)} + \frac{f(x_1) - f(x_0)}{2(x_1 - x_0)}$$

Catmull-Rom spline

$$\dot{f}(x_1) \approx \frac{f(x_2) - f(x_0)}{x_2 - x_0}$$

$$Q_1 = (x_1, f(x_1)) \qquad \dot{f}(x_1)$$

$$Q_2 = (x_2, f(x_2)) \qquad \dot{f}(x_2)$$

Let $P = (x, g(x))$ and $t = (x - x_1)/(x_2 - x_1)$,

$$g(x) = h_{00}(t) f(x_1) + h_{10}(t) \dot{f}(x_1)(x_2 - x_1) + h_{01}(t) f(x_2) + h_{11}(t) \dot{f}(x_2)(x_2 - x_1)$$

Example 1.3. Different Interpolation

B=imsize(A, 0.1, ‘nearest’);

original

nearest

bilinear

bicubic

Image Interpolation

Spline interpolation for 1D Data

$$\acute{A}(x) = \acute{A}^{\text{spline}}(x) = \mathring{a}_{l=1}^{m} c_l b^l(x)$$

$$\Im(x_j) = \text{DataT}(x_j) = \sum_{l=1}^{m} c_l b^l(x_j) \quad \text{for} \quad j = 1, \cdots, n$$

$$\text{DataT} = [b^1(\text{xc}), \cdots, b^m(\text{xc})](c_1, \cdots, c_m)^T = B_m \tilde{c}$$

Image Interpolation

Spline interpolation for d-D Data

$$\Im(x) = \Im^{\text{spline}}(x) = \sum_{l_1=1}^{m_1} \cdots \sum_{l_d=1}^{m_d} c_{l_1,\cdots,l_d} b^{l_1}(x^1) \cdots b^{l_d}(x^d)$$

$$\Im(x_j) = \text{DataT}(x_j) = \sum_{l_1=1}^{m_1} \cdots \sum_{l_d=1}^{m_d} c_{l_1,\cdots,l_d} b^{l_1}(x_j^1) \cdots b^{l_d}(x_j^d) \quad \text{for} \quad j = 1,\cdots,n$$

$$\text{DataT} = B_m \tilde{c} = B_{m^d} \otimes \cdots \otimes B_{m^1} \tilde{c}$$

$$\partial_{x^q} \Im(x) = \Im^{\text{spline}}(x) = \sum_{l_1=1}^{m_1} \cdots \sum_{l_d=1}^{m_d} c_{l_1,\cdots,l_d} b^{l_1}(x^1) \cdots \partial_{x^q}[b^{l_q}(x^q)] \cdots b^{l_d}(x^d)$$

Image Representation

The objective is to find a function

$$\mathrm{DataT}(x_j) = \Im(x_j) + \varepsilon(x_j) \quad \text{for} \quad j = 1, \cdots, n$$

$$\Im(x) = \mathrm{inter}(\mathrm{T}, \mathrm{W}, \mathrm{xc})$$

$$\acute{A}(\square) = \mathrm{argmin}_{\acute{A}(.)} \{ \| \mathrm{DataT} - \acute{A}(\mathrm{xc}) \|^2 + / \, r(\acute{A}) \}$$

$/ = 0$ yields the interpolation problem.

$/ \to \infty$ yields a very smooth solution.

Example on spline

$$\acute{A}(x) = \acute{A}^{\mathrm{spline}}(x) = \sum_{l=1}^{m} c_l b^l(x)$$

$$\rho(\Im) = \int \{ d^2 \Im(x) \}^2 dx = \tilde{c}^T M \tilde{c}$$

Image Representation

$$(B^T B + \lambda W)\tilde{c} = B^T \mathrm{DataT}$$

Spline: $W = M$

Tychonoff regularization: $W = I$

Tychonoff-Phillips regularization: $W = D^T D$

- E3_MS_splineInterpolation2D
- E3_US_getMultilevel
- E3_splineInterpolation2D

Image Representation

/ = 0

/ = 1000

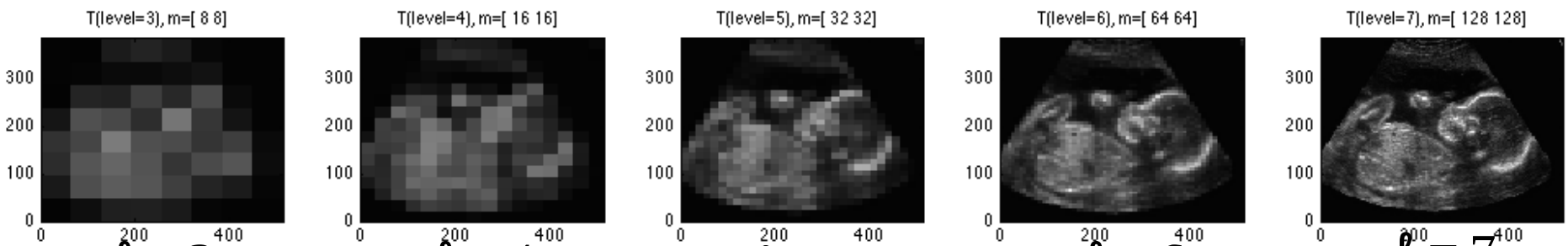
/ = 10

Image Representation

A multilevel approach is to use a finite number of interpolants $\acute{A}_\ell$ based on data $(\mathrm{xc}^\ell, T^\ell)$, where the discrete parameter ℓ ranges from a coarse to a fine level.

Example Let $m = 2^L, L \in N$ and dataT $\in R^m$. A multilevel representation of the data is $\{T^\ell : \ell = 0, \cdots, L\}$, where $T^L =$ dataT and for all $\ell = L:-1:1$, we have

$$T^{\ell-1} = (T^\ell(1:2:m-1) + T^\ell(2:2:m))/2$$



$\ell = 3$ $\ell = 4$ $\ell = 5$ $\ell = 6$ $\ell = 7$

Imaging Denoising/Filter

- An image may be “dirty” (with dots, speckles,stains)
- Noise removal:
  - To remove speckles/dots on an image
  - Dots can be modeled as impulses (salt-and-pepper or speckle) or continuously varying (Gaussian noise)
  - Can be removed by taking mean or median values of neighboring pixels (e.g. 3x3 window)
  - Equivalent to low-pass filtering
- Problem with low-pass filtering
  - May blur edges
  - More advanced techniques: adaptive, edge preserving

Thanks Yao Wang

Point Spreading Function

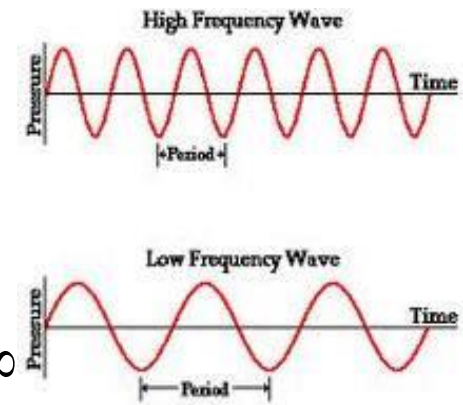
A 2D point spreading function (PSF) K(x, y) is a smooth function satisfying

(preserve low frequency)

- $\iint_{R^2} K(x,y)\,dx\,dy = 1$ **or** $\hat{K}(0,0) = 1$

(suppress high frequency)

- $\hat{K}(w_1, w_2)$ **decays sufficiently fast as** $|\omega| \to \infty$



2D Fourier transform

$$\hat{K}(w_1, w_2) = \iint_{R^2} K(x,y)\, e^{-i(w_1 x + w_2 y)}\,dx\,dy$$

Lowpass condition

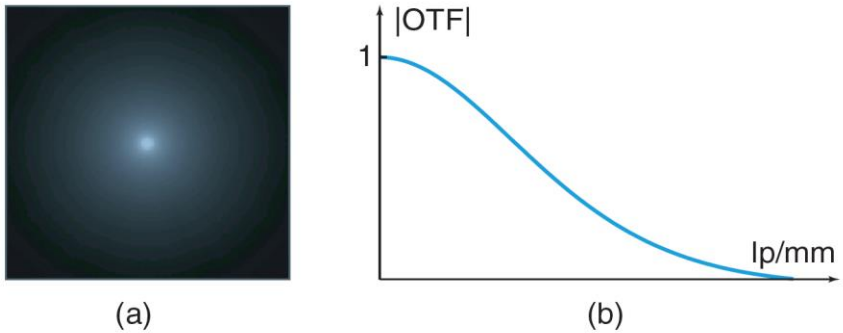


Figure 1.5 **(a)** Point spread function (PSF). **(b)** Corresponding modulation transfer function (MTF). The MTF is the amplitude of the optical transfer function (OTF), which is the Fourier transform (FT) of the PSF.

- **A *radially* symmetric PSF K is *isotropic***

$$K(x,y) = k(x^2 + y^2) \qquad K(x,y) = k(x^2 + y^2) = \exp(-(x^2+y^2)/(2s^2))/(2ps^2)$$

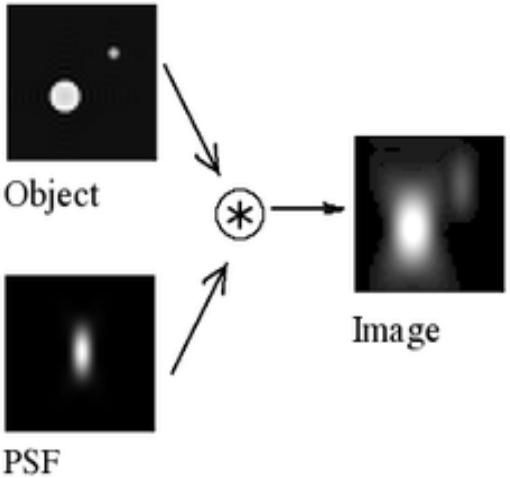
PSF is *orientation selective or polarized*, if

$$K(x,y) = k((x,y)A(x,y)^T) \qquad K(x,y) = \exp(-(x,y)A(x,y)^T)/(2p|A|^{1/2})$$

- **A nonnegative PSF** $K(x,y) \geq 0$ **is a PDF.**

- **Convolution is given by**

$$\tilde{f}(x,y) = K * f(x,y) = \int_{\Omega} K(x-p, y-q) f(p,q)\,dp\,dq.$$



Weighted Averaging Filter

- Instead of averaging all the pixel values in the window, give the closer-by pixels higher weighting, and far-away pixels lower weighting.

$$\tilde{f}(x,y) = K * f(x,y) = \int_{\Omega} K(x-p, y-q) f(p,q)\,dp\,dq.$$

- This type of operation for arbitrary weighting matrices is generally called "2-D convolution or filtering". When all the weights are positive, it corresponds to weighted average.
- Weighted average filter retains low frequency and suppresses high frequency = low-pass filter

Weighted Averaging Filter

$\frac{1}{9}\times$

1	1	1
1	1	1
1	1	1

100	100	100	100	100
100	200	205	203	100
100	195	200	200	100
100	200	205	195	100
100	100	100	100	100

$\frac{1}{16}\times$

1	2	1
2	4	2
1	2	1

100	100	100	100	100
100	144	167	145	100
100	167	200	168	100
100	144	166	144	100
100	100	100	100	100

100	100	100	100	100
100	156	176	158	100
100	174	201	175	100
100	156	175	156	100
100	100	100	100	100

Median Filter

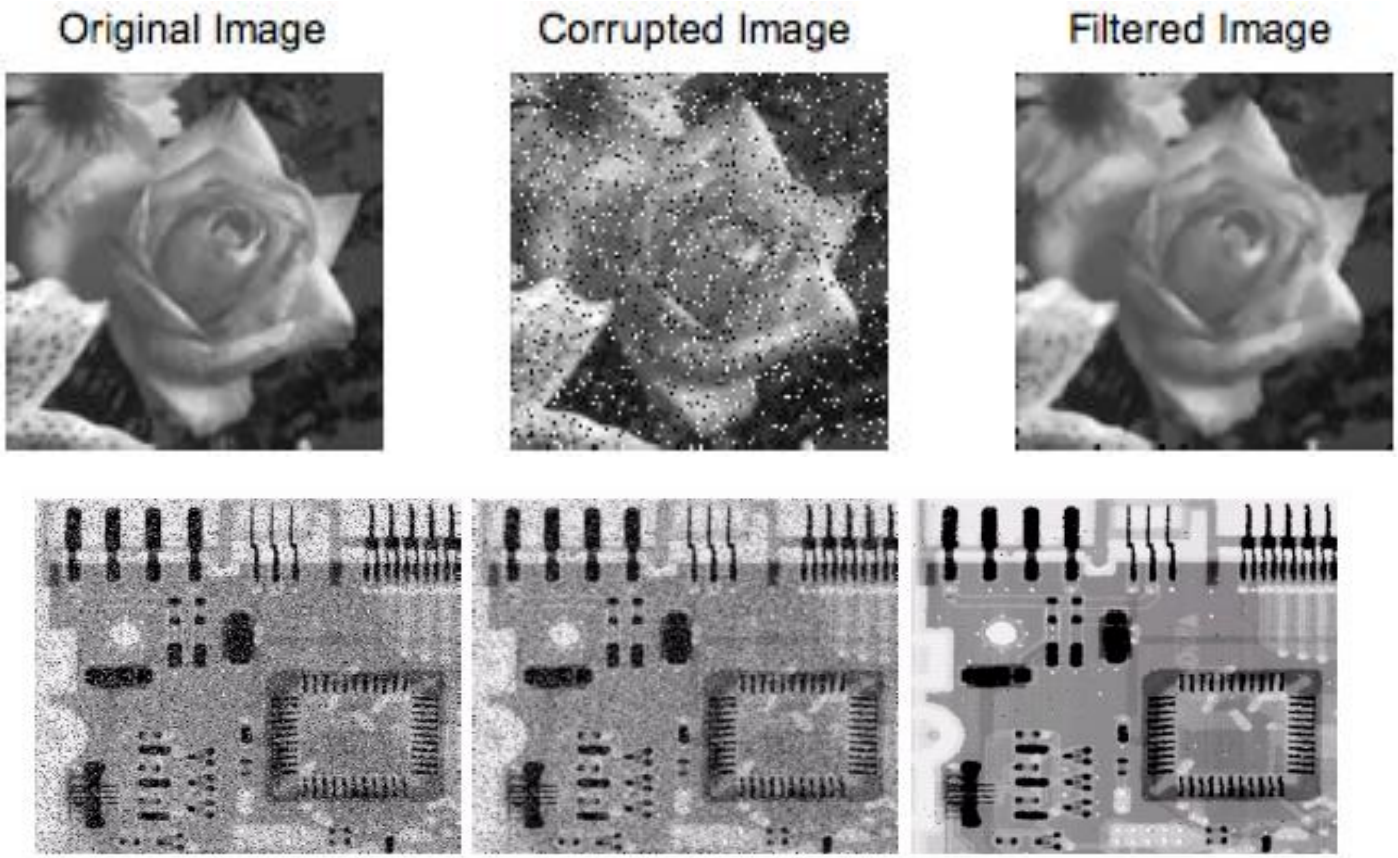
- Problem with Averaging Filter
  - Blur edges and details in an image
  - Not effective for impulse noise (Salt-and-pepper)
- Median filter:
  - Taking the median value instead of the average or weighted average of pixels in the window
    - Median: sort all the pixels in an increasing order, take the middle one
  - The window shape does not need to be a square
  - Special shapes can preserve line structures
- Order-statistics filter
  - Instead of taking the mean, rank all pixel values in the window, take the n-th order value.
  - E.g. max or min

100	100	100	100	100
100	200	205	203	100
100	195	200	200	100
100	200	205	195	100
100	100	100	100	100

100	100	100	100	100
100	100	200	100	100
100	200	200	200	100
100	100	195	100	100
100	100	100	100	100

Matlab command: medfilt2(A,[3 3])

Median Filter



a b c

FIGURE 3.37 (a) X-ray image of circuit board corrupted by salt-and-pepper noise. (b) Noise reduction with a 3×3 averaging mask. (c) Noise reduction with a 3×3 median filter. (Original image courtesy of Mr. Joseph E. Pascente, Lixi, Inc.)

Highpass Filters

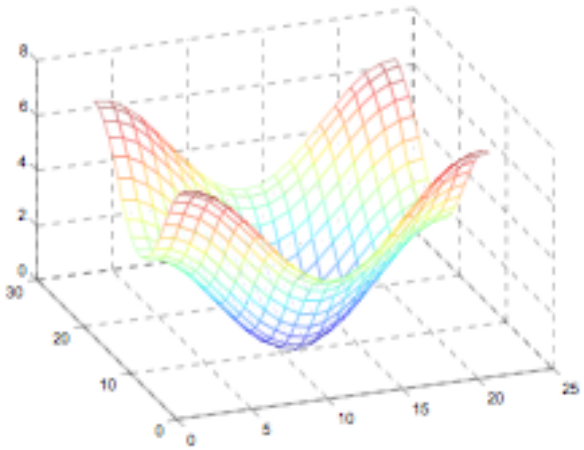
- Spatial operation: taking difference between current and averaging (weighted averaging) of nearby pixels
  - Can be interpreted as weighted averaging = linear convolution
  - Can be used for edge detection
- Example filters

$$\begin{bmatrix} 0 & 1 & 0 \\ 1 & -4 & 1 \\ 0 & 1 & 0 \end{bmatrix}; \quad \begin{bmatrix} 0 & -1 & 0 \\ -1 & 4 & -1 \\ 0 & -1 & 0 \end{bmatrix}; \quad \begin{bmatrix} 1 & 1 & 1 \\ 1 & -8 & 1 \\ 1 & 1 & 1 \end{bmatrix}; \quad \begin{bmatrix} -1 & -1 & -1 \\ -1 & 8 & -1 \\ -1 & -1 & -1 \end{bmatrix};$$

  - All coefficients sum to 0!

Highpass Filters

$$\begin{bmatrix} 0 & -1 & 0 \\ -1 & 4 & -1 \\ 0 & -1 & 0 \end{bmatrix}$$



Original image

Isotropic edge detection

Image Segmentation

Slide: G. Gerig

Image Segmentation:
Subdivision of image data
Into "meaningful" entities
(objects, regions, boundaries).

= partitioning into disjoint object sets
(based on region properties)

There are other objects worthwhile segmenting (e.g., graphs to analyze social networks), but I won't talk about this today.

Image Segmentation

Image Segmentation bridges between low-level vision/image processing and high-level vision. Its goal is to cluster a given Image into a collection of 'objects', and then other high-level tasks such as object detection, recognition, and tracking can be performed.

Definition: $I : \Omega \rightarrow M \qquad \Omega \subset R^2 \text{ or } R^3$

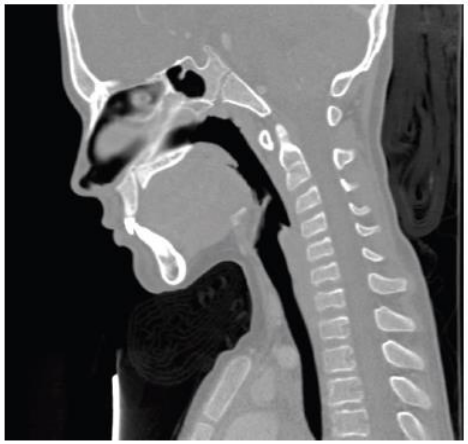
$\{\Omega_i : i = 1, \cdots, N\}$ such that

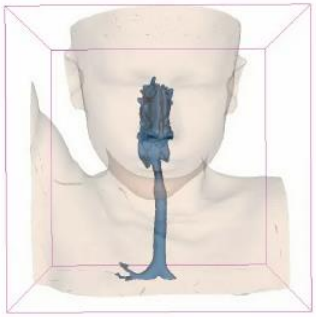
(i) $\Omega_i \cap \Omega_j = \phi$ for $i \neq j$;

(ii) $\Omega = \Omega_1 \cup \Omega_2 \cup \cdots \cup \Omega_N \cup \Gamma$ with $\Gamma = \cup_{i=1}^{N} \partial\Omega_i$

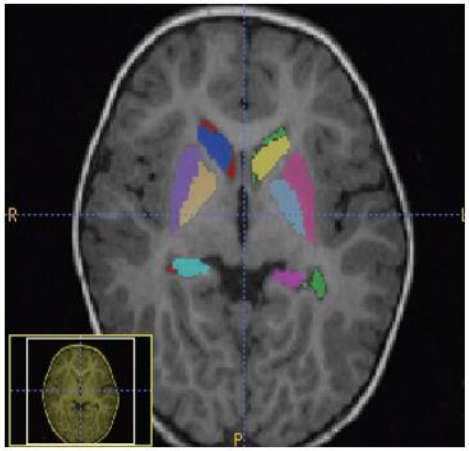
Examples

Example: Airway Segmentation from CT

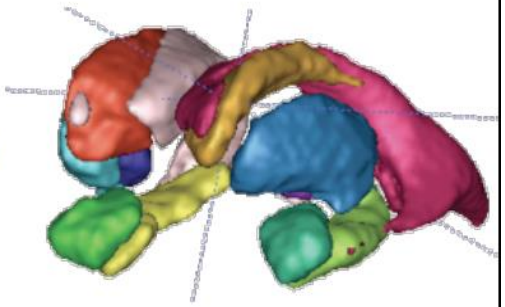




Example: Automatic Segmentation of the Brain



structural MRI of the brain



Subcortical structures

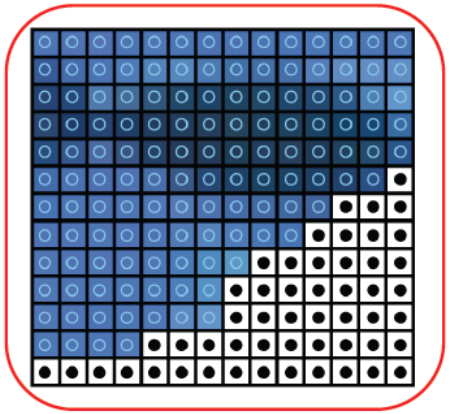
Statistical Image Segmentation

Observed Image/features

$$Y = \{y(w) : w \in \Omega\}$$

Classification Image

$$X = \{x(w) : w \in \Omega\}$$



Likelihood Function

$$p(Y \mid X)$$

Prior (local smooth)

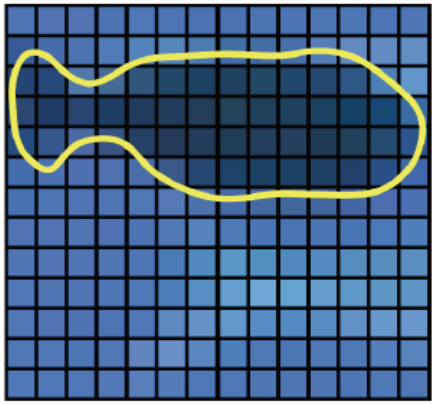
$$p(X)$$

Bayesian Rule

$$p(X \mid Y) = p(Y \mid X)p(X) / p(Y)$$

Inference

$$\hat{X} = \{\hat{x}(w) : w \in \Omega\} \Rightarrow \bigcup_{i=1}^{N} \Omega_i \cup \Gamma$$



Example: Gaussian Mixture Normal

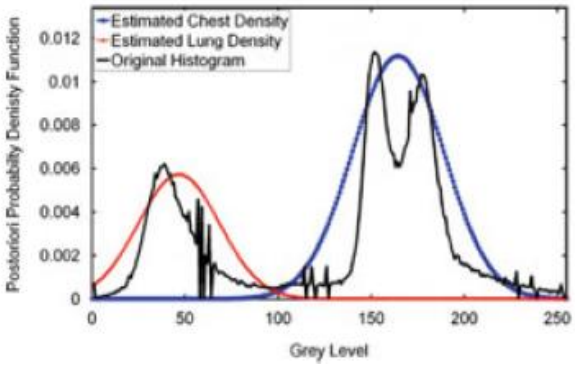
$$p(Y \mid X) = \prod_{d \in D} N(y(d); \mu_{x(d)}, \sigma^2_{x(d)})$$

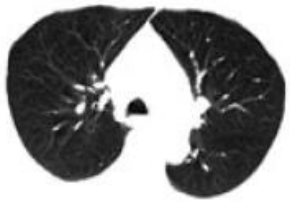
$$p(X) = \prod_{d \in D} \prod_{k} p_k^{1(x(d)=k)}$$

$$p(Y) = \prod_{d \in D} \sum_{k=1}^{K} p_k N(y(d); \mu_k, \sigma_k^2)$$

Initial CT chest slice

Ground truth (hand-drawn lungs)





Deformable Model Segmentation

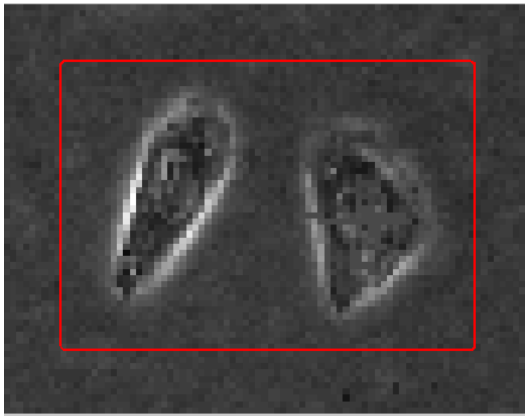
Deformable models are curves or surfaces, for segmentation in the image domain, or hyper-surfaces, for the segmentation of higher dimensional image.

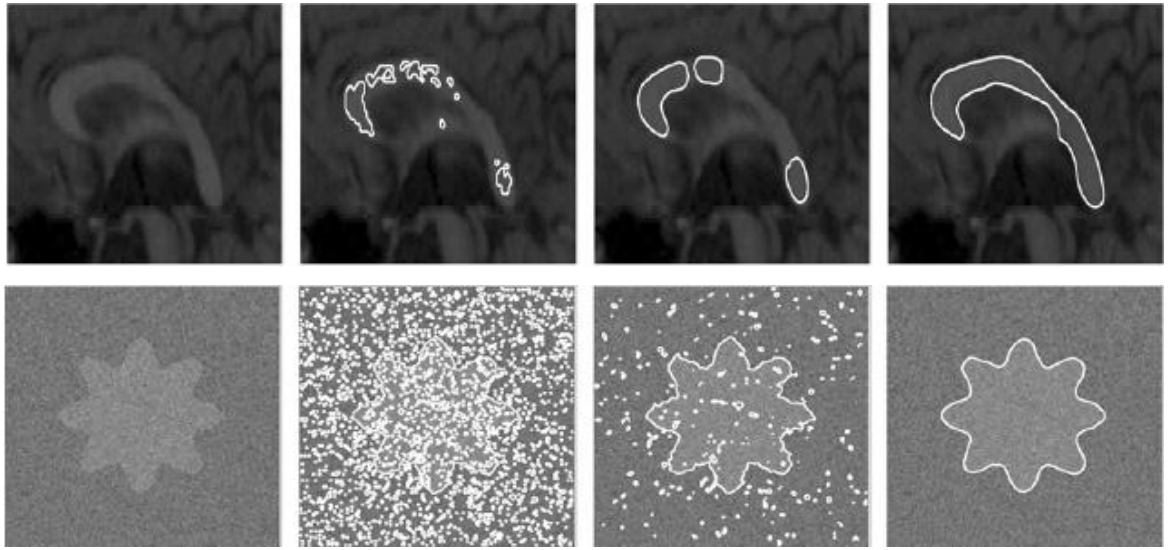
$$\Gamma = \bigcup_{i=1}^{N} \partial\Omega_i \qquad p(Y \mid X; \mathsf{G})\, p(X; \mathsf{G}) \Rightarrow \hat{\Gamma} = \bigcup_{i=1}^{N} \partial\hat{\Omega}_i$$

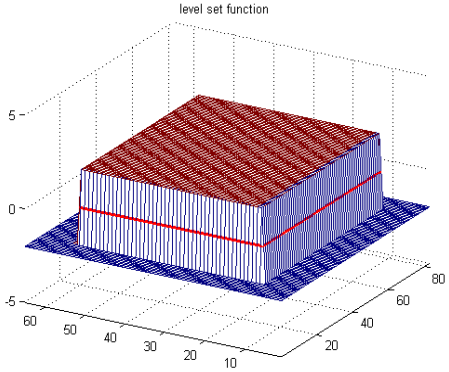
Parametric Active Contours (Kass et al 1987) $\mathcal{C}(s) = [x(s), y(s)]$

$$E = \int_0^1 \frac{1}{2}(\alpha|\mathcal{C}'(s)|^2 + \beta|\mathcal{C}''(s)|^2)ds + \int_0^1 E_{\text{ext}}(\mathcal{C}(s))ds \qquad E_{\text{ext}}(x,y) = -|\nabla(G_\sigma * I(x,y))|^2$$

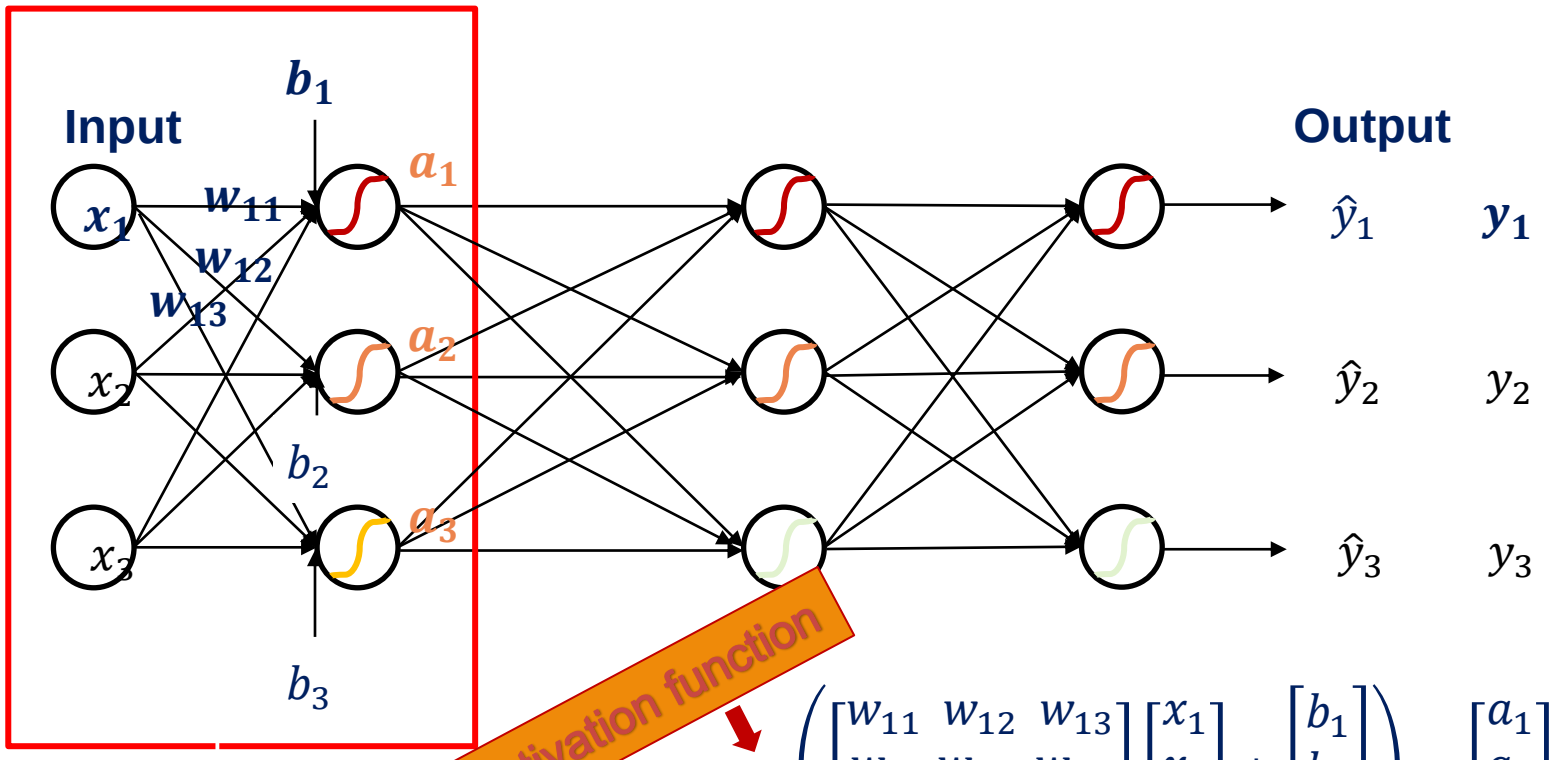
Examples







Neural Network

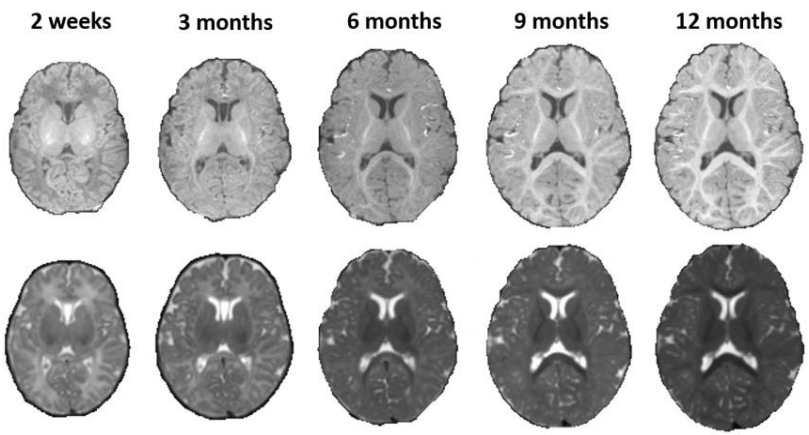


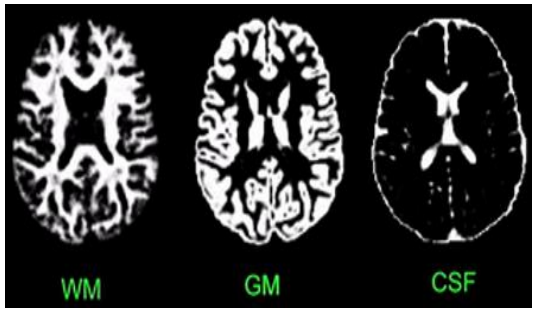
$$\sigma\left(\begin{bmatrix} w_{11} & w_{12} & w_{13} \\ w_{21} & w_{22} & w_{23} \\ w_{31} & w_{32} & w_{33} \end{bmatrix}\begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} + \begin{bmatrix} b_1 \\ b_2 \\ b_3 \end{bmatrix}\right) = \begin{bmatrix} a_1 \\ a_2 \\ a_3 \end{bmatrix}$$

Matrix Operation

Example: U-net based Segmentation

Design a method to promote automatic segmentation algorithms on the 6-months infant brain MRI into white matter (WM), gray matter (GM), and cerebrospinal fluid (CSF) by utilizing T1- and T2-weighted brain MRI scans. The 6-month infant brain, which is also named by the isointense-phase infant brain, has the major difficulty to segment for its overlapping of GM and WM and the lowest tissue contrast.





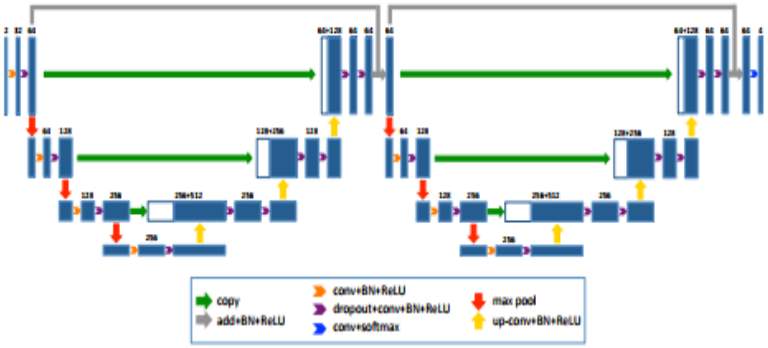


Fig. 1. The 3D GlassesNet architecture. Each box represents a set of 3D feature maps. The number of 3D feature maps is denoted above the box.

Table 2: *The average Dice's coefficients over 13 testing samples*

Rank	Team	WM	GM	CSF
	BIGS2 (**GlassesNet**)	**0.909** (p=1.9e-6)	**0.928** (p=3.5e-7)	**0.961** (p=1.3e-5)
1	MSL_SKKU	0.904	0.923	0.958
2	LIVIA	0.897	0.919	0.957
3	Bern_IPMI	0.896	0.916	0.954
5+	BIGS2 (LFA-CNN)	0.867	0.892	0.948

$$\text{Dice's coefficient} = \frac{2|X \cap Y|}{|X| + |Y|}$$

Image Registration

Image registration is the process of transforming different sets of data into *one coordinate system*. Data may be multiple photographs, data from different sensors, from different times, or from different viewpoints.

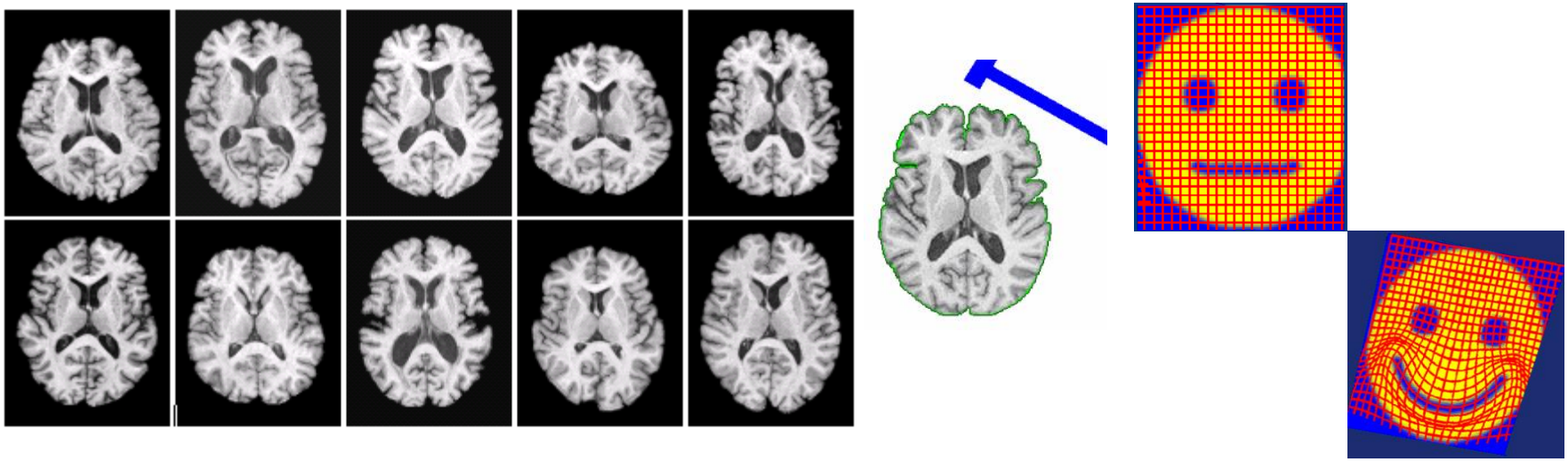


Image Transformations

Recall Contrast Enhancements $\tilde{f}(i,j) = T[f(i,j)]$

$$\tilde{f}(\tilde{x}) = T[f(\tilde{x})], \quad \text{for all } \tilde{x} \in \Omega$$

$$\text{when } T[\tilde{y}] \text{ is a monotonic function of } \tilde{y}.$$

Deformation

$$\tilde{f}(\tilde{x}) = f(T(\tilde{x})), \quad \text{for all } x \in \Omega$$

$$\text{when } \tilde{x}' = T(\tilde{x}) \text{ is a one-to-one transformation of } \tilde{x}.$$

Image Registration

Given two images $\mathfrak{I},\mathfrak{R}:\mathrm{W}\subset R^d \to R$, find a transformation $T:R^d \to R^d$ such that

$$\hat{\mathrm{T}}=\mathrm{argmin}_T \mathrm{D}(\mathfrak{I}[T],\mathfrak{R})+S[T]$$

$\mathfrak{I},\mathfrak{R}:\mathrm{W}\subset R^d \to R$ denote template and reference images

$\acute{\mathrm{A}}[T](x)=\acute{\mathrm{A}}(T(x))$

$\mathrm{D}(\acute{\mathrm{A}}[T],\hat{\mathrm{A}})$ denotes a prefixed distance measure

$S[T]$ is a regularizer of T

Parameterized Transformations

Examples of $\tilde{x}' = T(\tilde{x})$

scaling $$\begin{pmatrix} x' \\ y' \\ 1 \end{pmatrix} = \begin{pmatrix} s_x & 0 & 0 \\ 0 & s_y & 0 \\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x \\ y \\ 1 \end{pmatrix}$$

translation $$\begin{pmatrix} x' \\ y' \\ 1 \end{pmatrix} = \begin{pmatrix} 1 & 0 & t_x \\ 0 & 1 & t_y \\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x \\ y \\ 1 \end{pmatrix}$$

shear $$\begin{pmatrix} x' \\ y' \\ 1 \end{pmatrix} = \begin{pmatrix} 1 & u_x & 0 \\ u_y & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x \\ y \\ 1 \end{pmatrix}$$

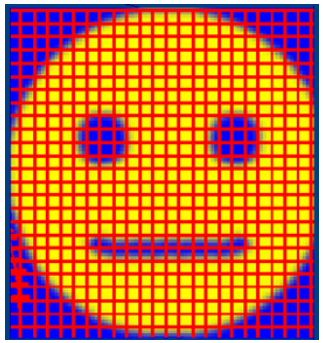
rotation $$\begin{pmatrix} x' \\ y' \\ 1 \end{pmatrix} = \begin{pmatrix} \cos\theta & -\sin\theta & 0 \\ \sin\theta & \cos\theta & 0 \\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x \\ y \\ 1 \end{pmatrix}$$

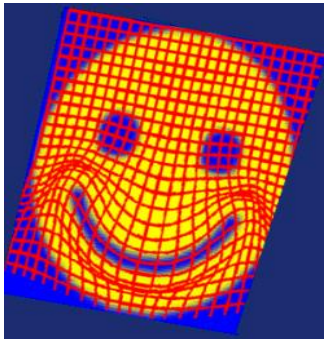
general affine $$\begin{pmatrix} x' \\ y' \\ 1 \end{pmatrix} = \begin{pmatrix} a_{11} & a_{12} & t_x \\ a_{21} & a_{22} & t_y \\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x \\ y \\ 1 \end{pmatrix}.$$

Linear (Affine) Transformation

general affine $$\begin{pmatrix} x' \\ y' \\ z' \\ 1 \end{pmatrix} = \begin{pmatrix} a_{11} & a_{12} & a_{13} & t_x \\ a_{21} & a_{22} & a_{23} & t_y \\ a_{31} & a_{32} & a_{33} & t_z \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x \\ y \\ z \\ 1 \end{pmatrix}.$$

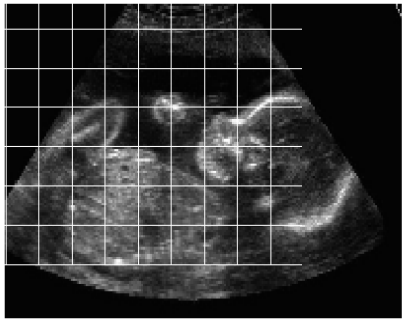
Nonlinear Transformation





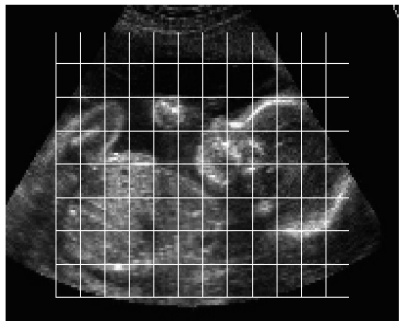
Parameterized Transformations

interpolated data, m=[192 128]



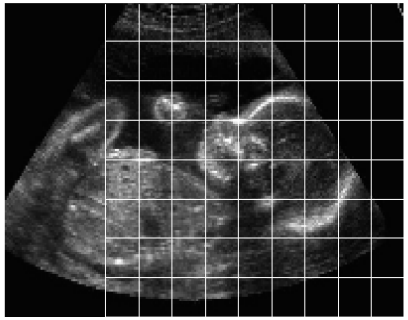
translation

interpolated data, m=[192 128]



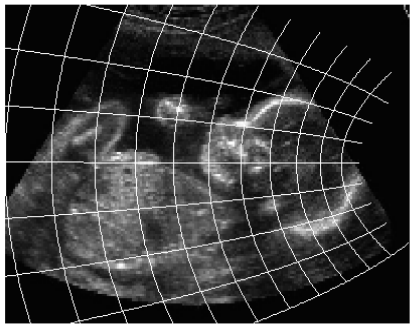
scale

interpolated data, m=[192 128]



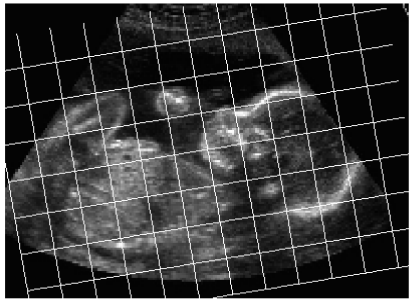
translation-x1

interpolated data, m=[192 128]



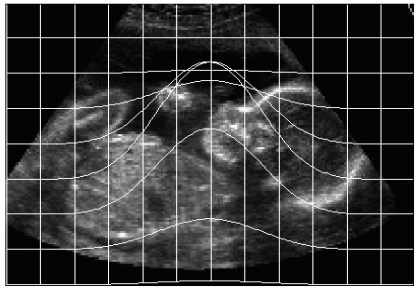
non-linear

interpolated data, m=[192 128]



rotation

interpolated data, m=[192 128]



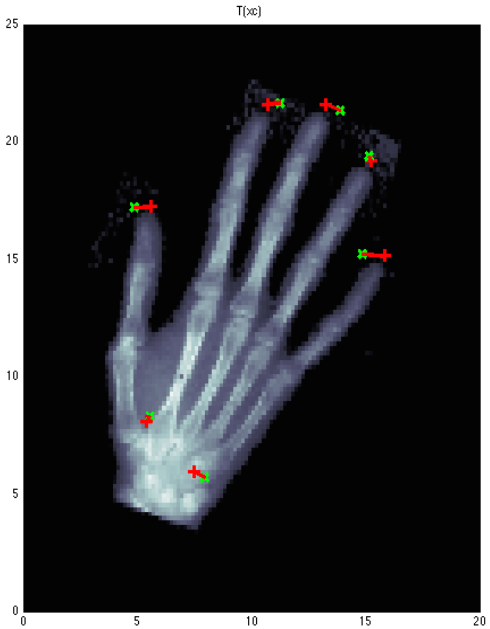
spline

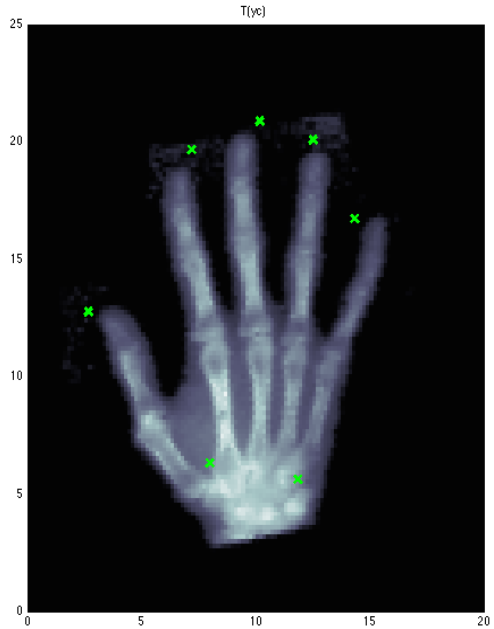
Landmark-based Registration

Given two images $\mathfrak{I},\mathfrak{R}:W\subset R^d \to R$, find a transformation $T:R^d \to R^d$ such that

$$\hat{T}=\mathrm{argmin}_T D(\mathfrak{I}[T],\mathfrak{R})+S[T]$$

The basic idea of landmark-based registration is to determine the transformation such that for a finite number of features, any feature of the template image is mapped onto the corresponding feature of the reference image.





$$t_j=(t_j^1,\cdots,t_j^d)^T \in \Omega \text{ template image;}$$

$$r_j=(r_j^1,\cdots,r_j^d)^T \in \Omega \text{ reference image}$$

$$T(r_j)\approx t_j \text{ for } j=1,\cdots,m.$$

Landmark-based Registration

$$D^{LM}(\acute{A}[T],\hat{A}) = \sum_{j=1}^{m} \| T(r_j) - t_j \|_f^2$$

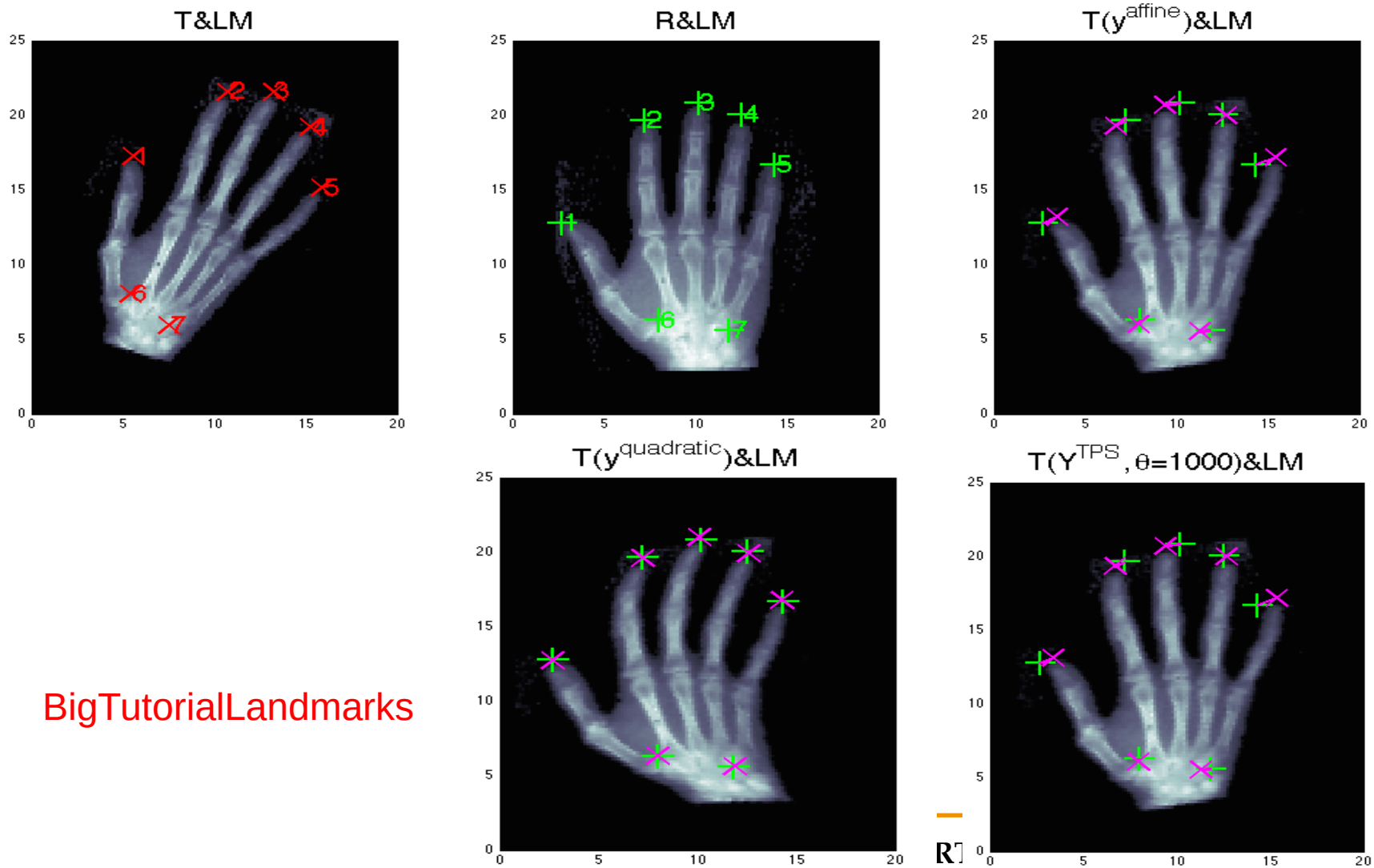
Regression: $T(r) = \sum_{j=1}^{m} a_j \psi_j(r)$ and $S[T] = 0$ e.g.,

$\{\psi_j(.)\}$ can be set as the basis functions of affine transformation

RKHS: $T(r) = \langle f, \Phi(r) \rangle_H$ and $S[T] = \lambda \| f \|_H^2$ e.g.,

$\{\Phi(.)\}$ denotes a feature map

Landmark-based Registration

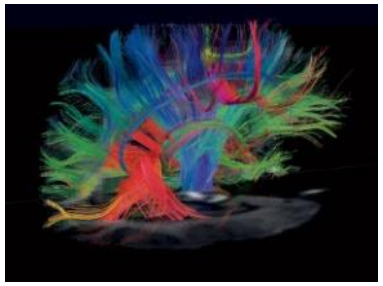


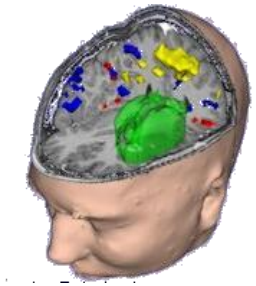
BigTutorialLandmarks

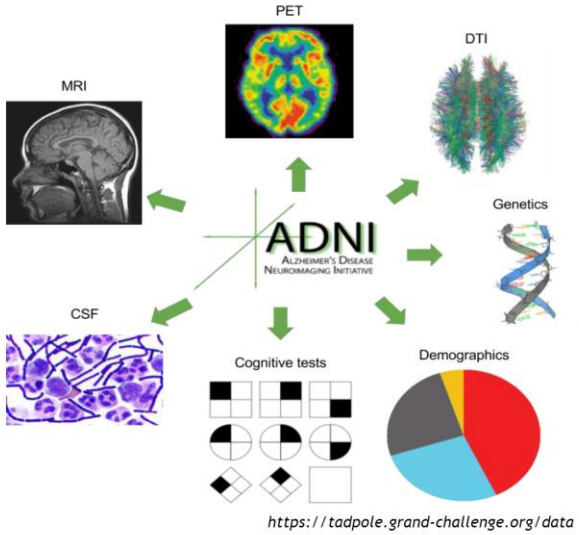
Part 4. Challenges

Major Challenges

- Annotation datasets
- Complex objects
- Complex spatial and/or temporal structures
- Extremely high dimensionality







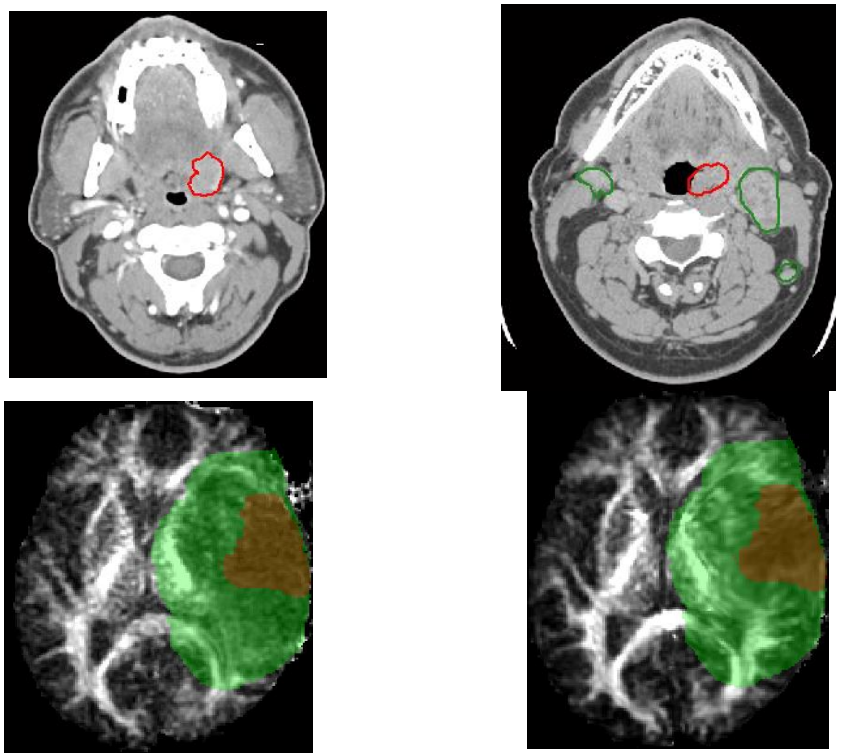
- Complicated causal pathways
- Complex missing patterns
- Heterogeneity across subjects, studies, and populations
- High dimensional variables across different domains
- Sampling bias

Data Challenges

IMAGENET

- Over 15M labeled high resolution images
- Roughly 80K categories
- Collected from web and labeled by Amazon Mechanical Turk

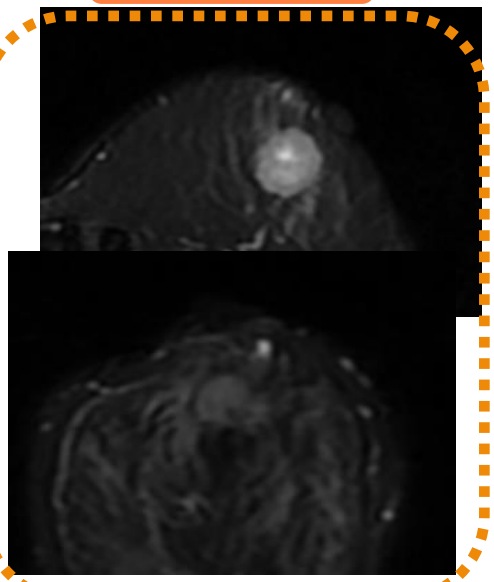
Lack of a large number of annotated data with high-quality



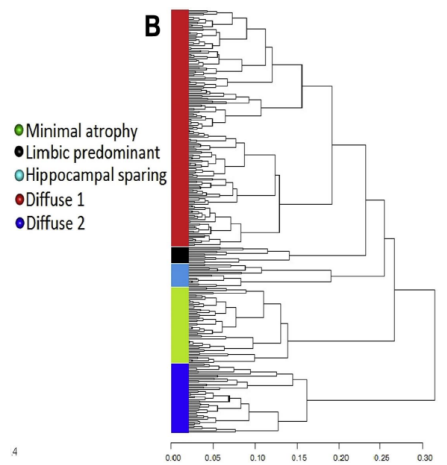
Heterogeneity Challenges

Heterogeneity at the subject, group, and study levels

Subject

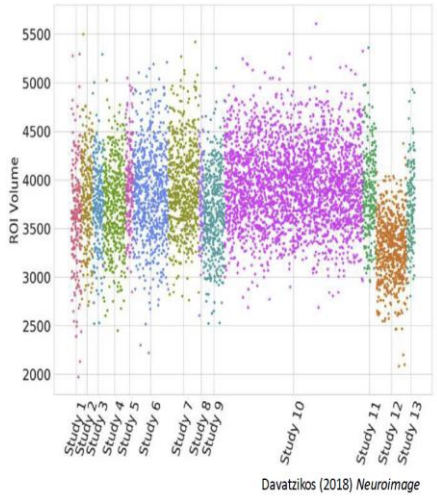


Group



Poulakis et al. (2018) *Neurobiol. Aging*

Study



Davatzikos (2018) *Neuroimage*

Integration Challenges

D

Healthcare

Genetics

Imaging

Clinical

Shallow Information

- Speech Recognition
- NLP
- Computer Vision

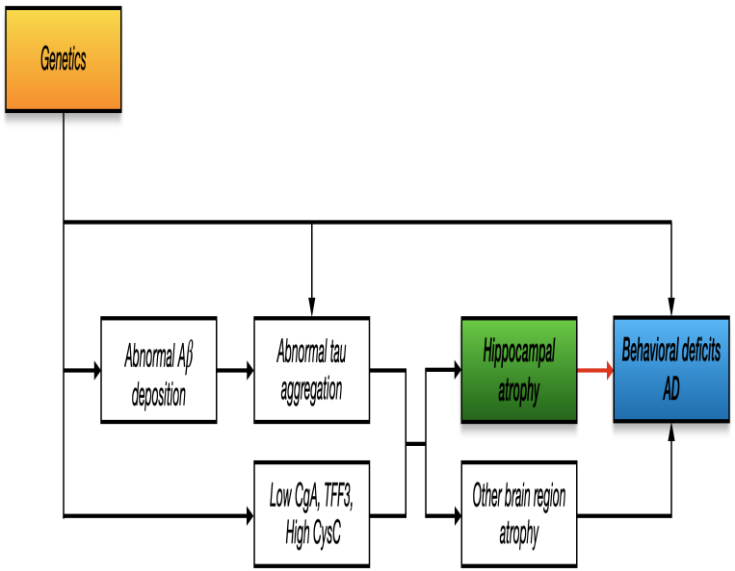
Prediction and Decision

IOT

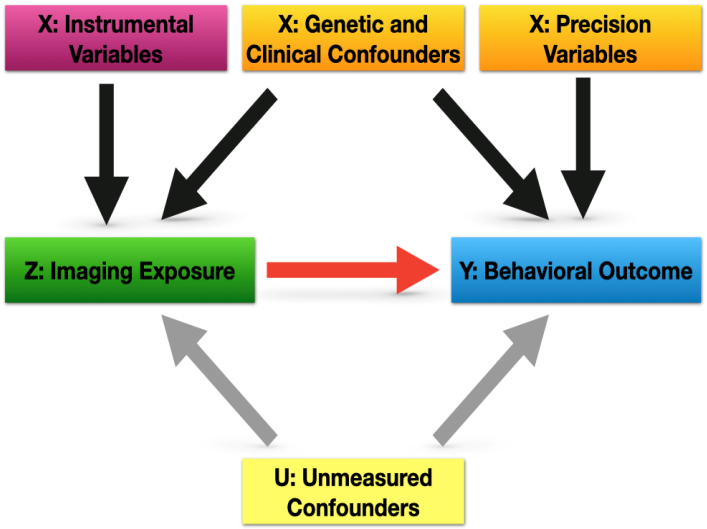
Source: 滴滴AI Labs, 滴滴战略部

https://qz.com/989137/when-a-robot-ai-doctor-misdiagnoses-you-whos-to-blame/

AD Pathogenesis



A hypothetical model of AD pathogenesis by Jack Jr et al. (2010).



Directed acyclic graph (DAG) of hippocampal exposure on dementia behavior