WMH Segmentation Challenge
Methods

Hugo Kuijf

UMC Utrecht

Problem: WMH segmentation

- What tool to use? What technique to implements? Is homemade better or not?

Problem: WMH segmentation

- What tool to use? What technique to implements? Is homemade better or not?

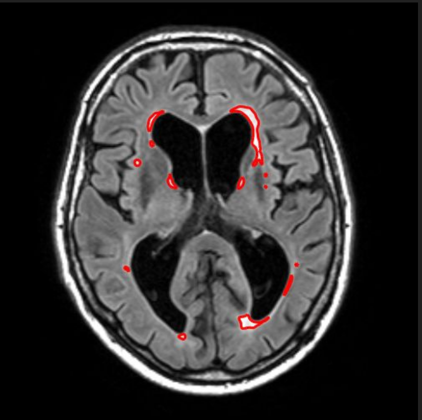
- Review by Caligiuri (2015):
  - Many techniques have been published: 34
  - Missing from review: 20+ (conference paper, too recent, MS)
- Issues:
  - Different ground truth, observers, inter-observer agreement
  - Different evaluation metrics
  - Different data sets

WMH Segmentation Challenge

Task: automatically segment WMH on brain MR images (T1 and FLAIR)

Data:

INSTITUTE	SCANNER	#TRAINING	#TEST
UMC Utrecht	3 T Philips Achieva	20	30
NUHS Singapore	3 T Siemens TrioTim	20	30
VU Amsterdam	3 T GE Signa HDxt	20	30
	3 T Philips Ingenuity	0	10
	1.5 T GE Signa HDxt	0	10



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WMH Segmentation Challenge

Task: automatically segment WMH on brain MR images (T1 and FLAIR)

Method:

- Participants download training data
- Tool is trained and containerized with Docker
- Organizer (me) runs all tools on all test data

Methods

UMC Utrecht

Teams: 20 teams have submitted their method

20 x 110 scans

40 CPUs and 4 GPUs

6 days of computation

Methods

Teams: 20 teams have submitted their method

<u>Up next: individual team power pitches</u>

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Automatic Segmentation of WMH using Multi-dimensional Gated Recurrent Units

Simon Andermatt, Simon Pezold, and Philippe Cattin

Department of Biomedical Engineering, University of Basel

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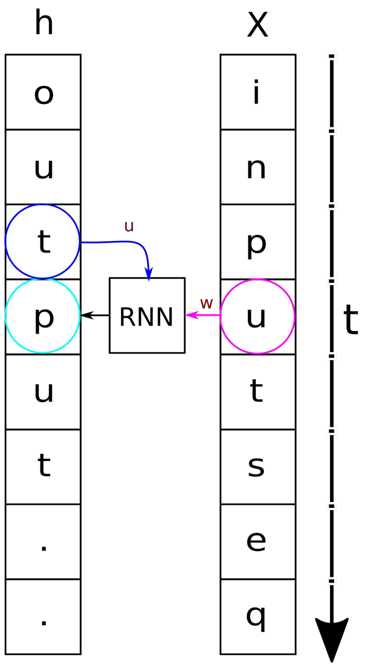
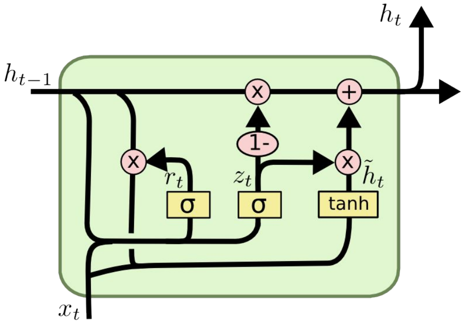
Recurrent Neural Networks

RNN



Gated Recurrent Unit (GRU)



$$z_t = \sigma\left(W_z \cdot [h_{t-1}, x_t]\right)$$

$$r_t = \sigma\left(W_r \cdot [h_{t-1}, x_t]\right)$$

$$\tilde{h}_t = \tanh\left(W \cdot [r_t * h_{t-1}, x_t]\right)$$

$$h_t = (1 - z_t) * h_{t-1} + z_t * \tilde{h}_t$$

Image credit: colah.github.io (Great tutorial on RNN)

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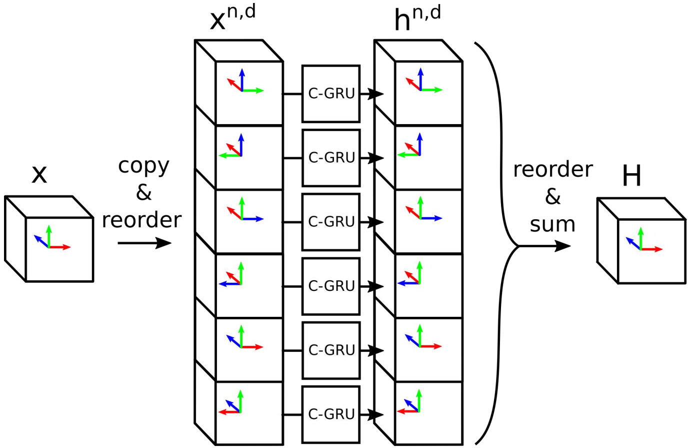
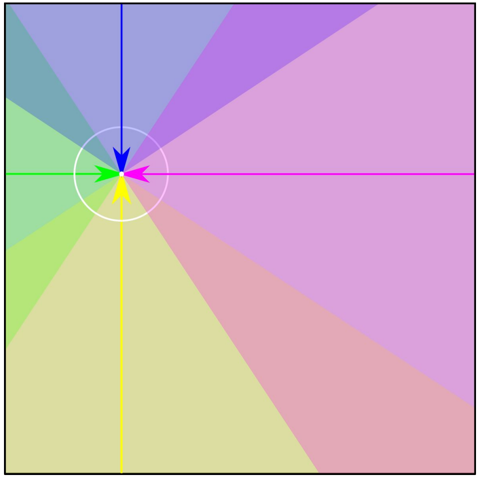
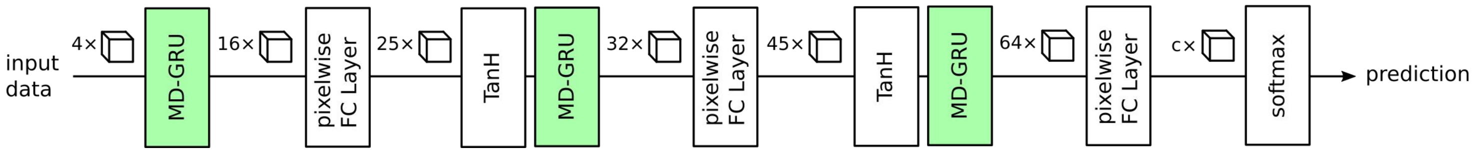
Multi-dimensional GRU (MD-GRU)







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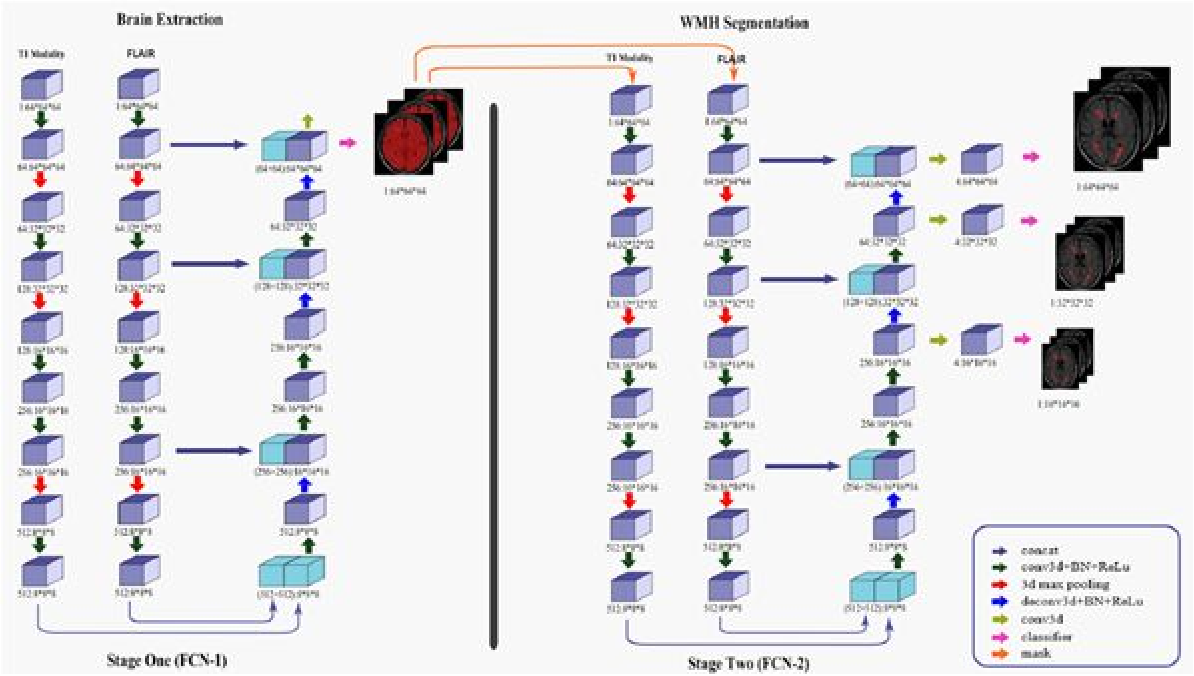
Deeply Supervised Multi-scale FCN for Segmentation of White Matter Hyperintensities (WMH)

Guodong Zeng and Guoyan Zheng, IPMI Lab., University of Bern, Switzerland



- Two-stages: FCN-1 for brain extraction and FCN-2 for WMH detection
- Long and short skip connections
- Multi-scale deep supervision

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I. Data Preprocessing

- Brain Extraction
  - Algorithm: FSL BET
- Removal of all-zero slices in z-direction.
- Resampling
  - (1 mm× 1 mm× original z spacing)
- Rescale intensity between [0, 1]
- Notes:
  - We used images pre/T1 and pre/FLAIR.
  - Only label value of 1 (white matter hyperintensity lesions) were used for training.

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II. Training

- Base Model
  - Architecture similar to 2D U-Net with 2 channel input (T1 and FLAIR).
  - 19 Convolutional Layers, 4 pooling layers, 4 upsampling layers.
  - Batch normalization layers after convolutional layers, ReLU as nonlinearity.
  - Output of last layer: Sigmoid.
  - Input Image Size: (348×348)
  - Output lesion label-map Size: (164×164)
- Models: trained 20 models based on the base model:
  - Training parameters: loss function: negative of Dice between prediction and ground truth labelmaps. Optimization: SGD with Adam update rule.
  - Multi-domain (general) models: 5-fold cross-validation on 60 images. Stratified sampling based on site/domain (Train: 15+15+15=45, Validation: 5+5+5=15)
  - Single-domain (domain specific) models: 5 fold cross-validation on each of the single domains: GE, Utrecht, and Singapore (total of 15 models).

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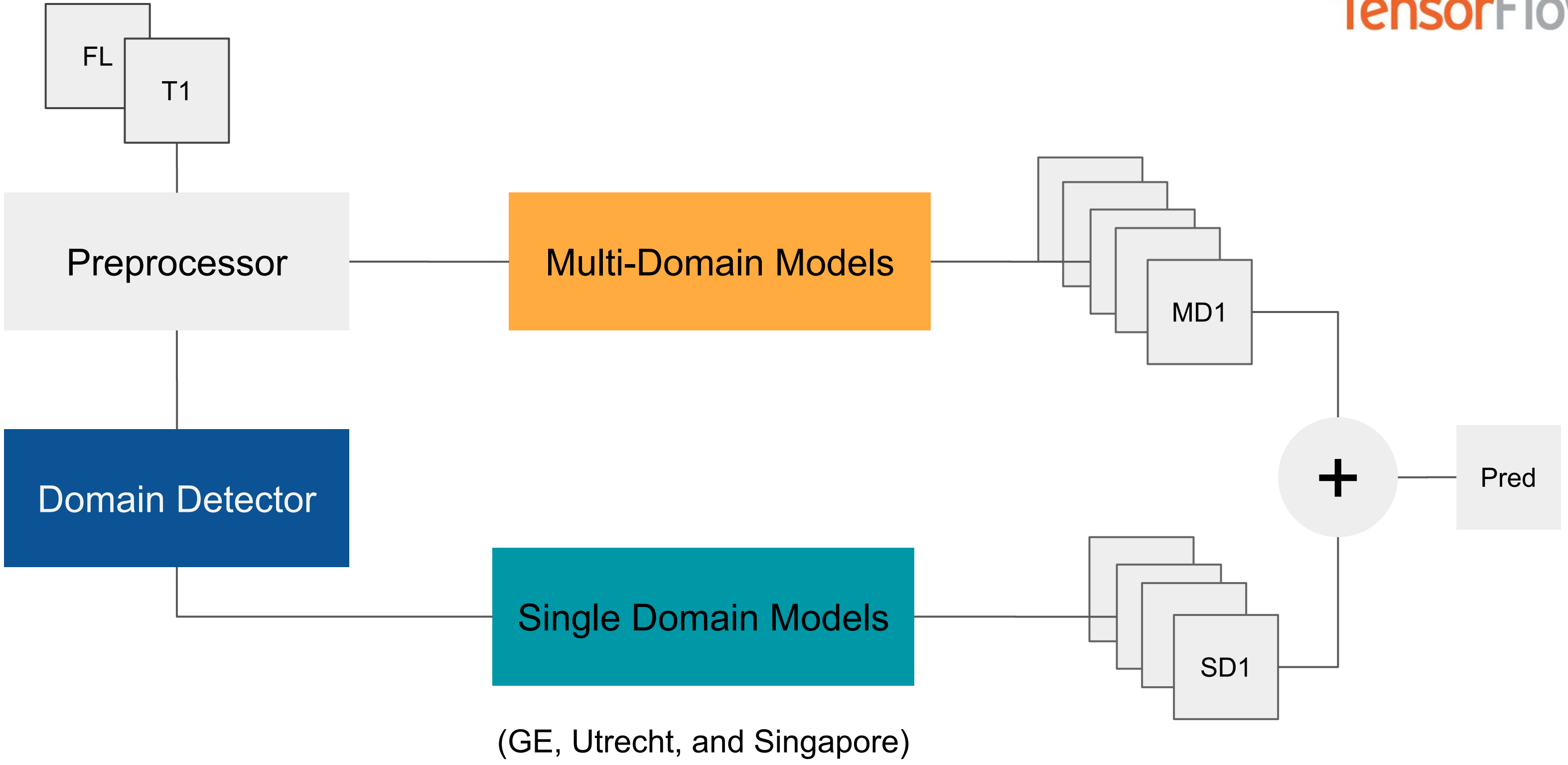
III. Deployment



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VLR: Voxel-Wise Logistic Regression

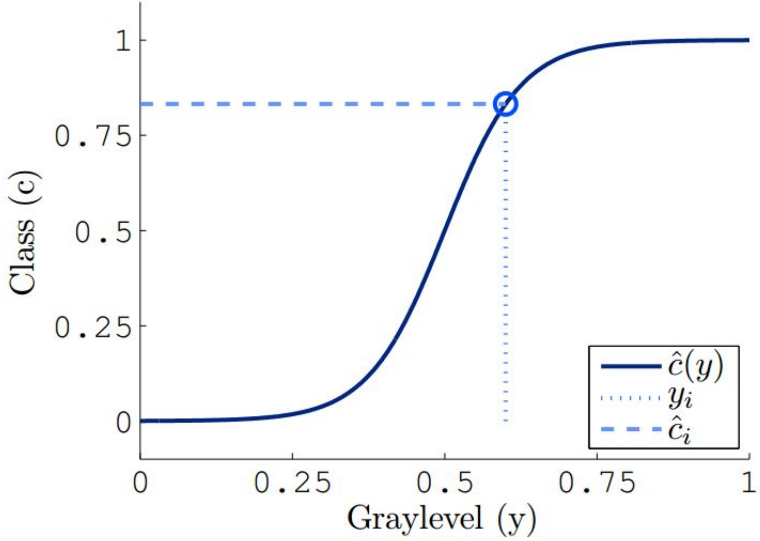
$$\hat{C}(x) = \frac{1}{1 + e^{-\eta(x)}}, \qquad \eta = \boldsymbol{\beta}(x)^T \boldsymbol{Y}(x)$$

$\hat{C}(x)$: Predicted class image

$\boldsymbol{\beta}(x)$: Logistic parameters

$\boldsymbol{Y}(x)$: Feature image(s)

For every voxel:



Jesse Knight, Graham Taylor, April Khademi

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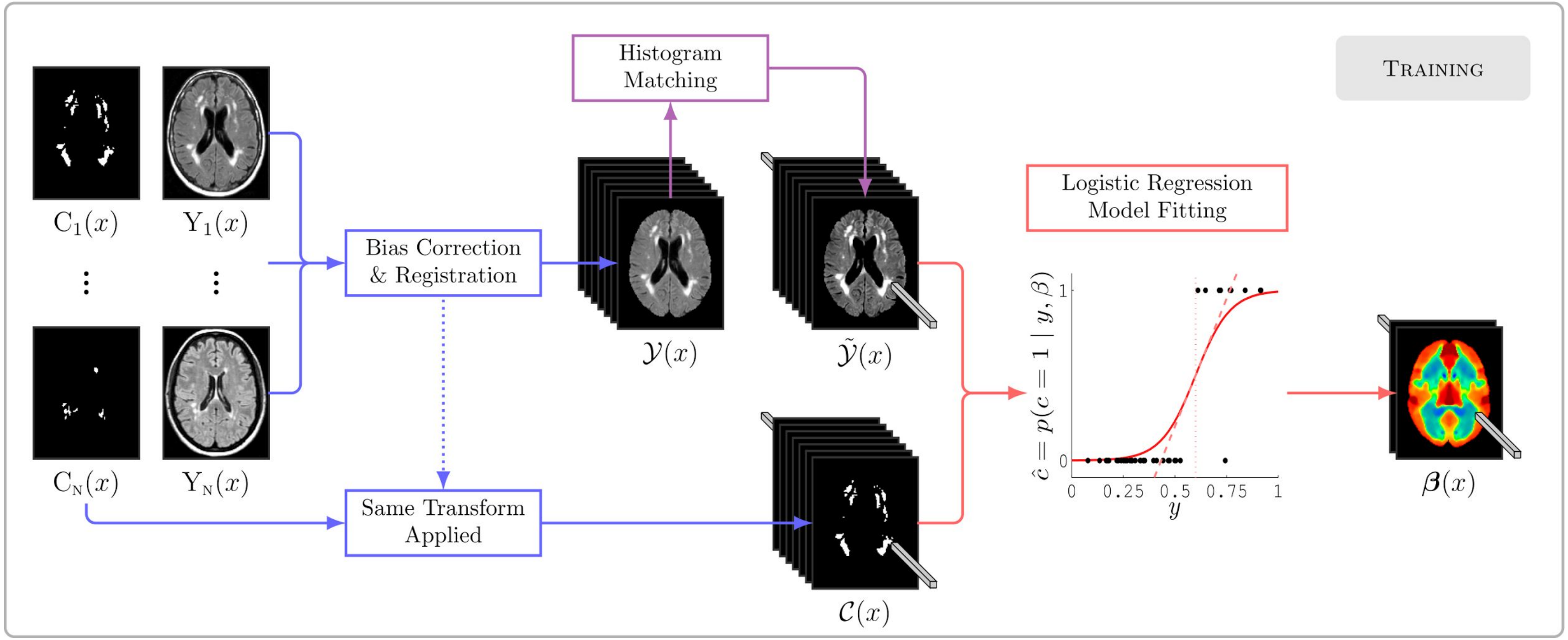
VLR: Training



Upright Roman: native space
Italic Roman: MNI space
Calligraphic: image set (MNI)

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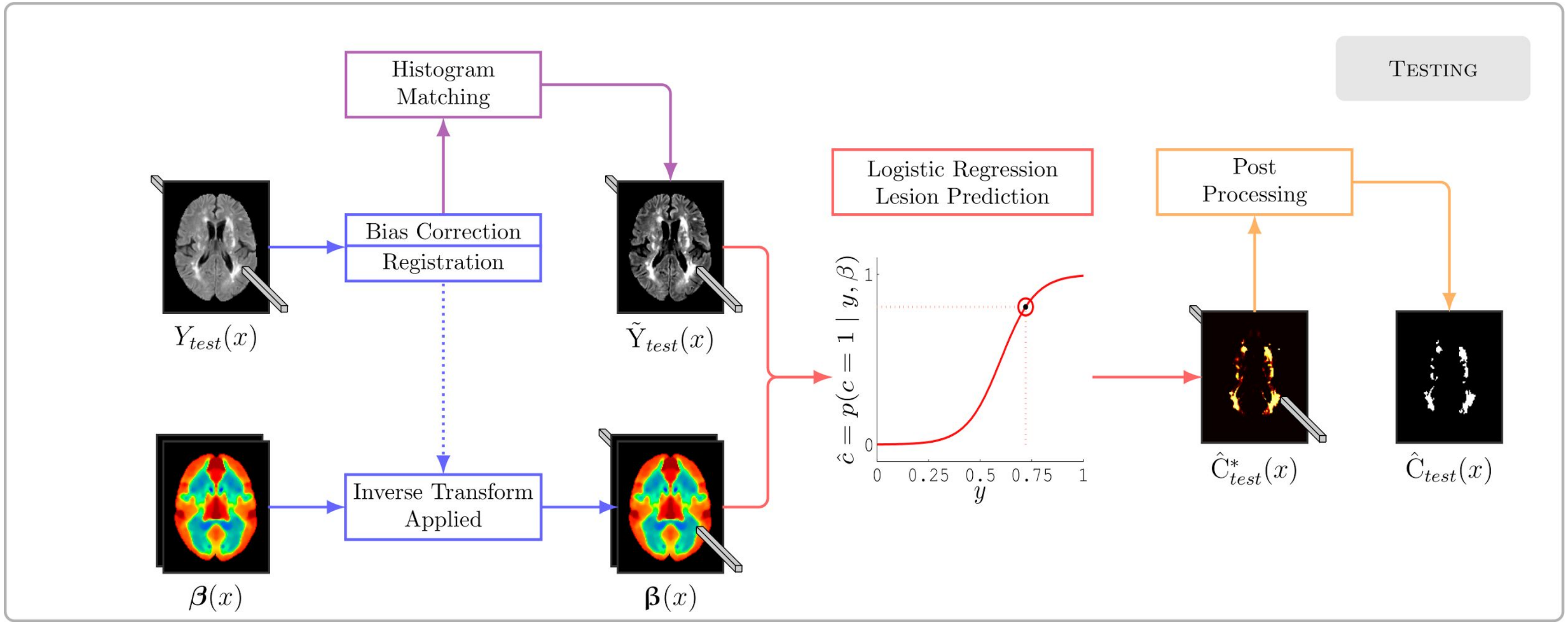
VLR: Testing



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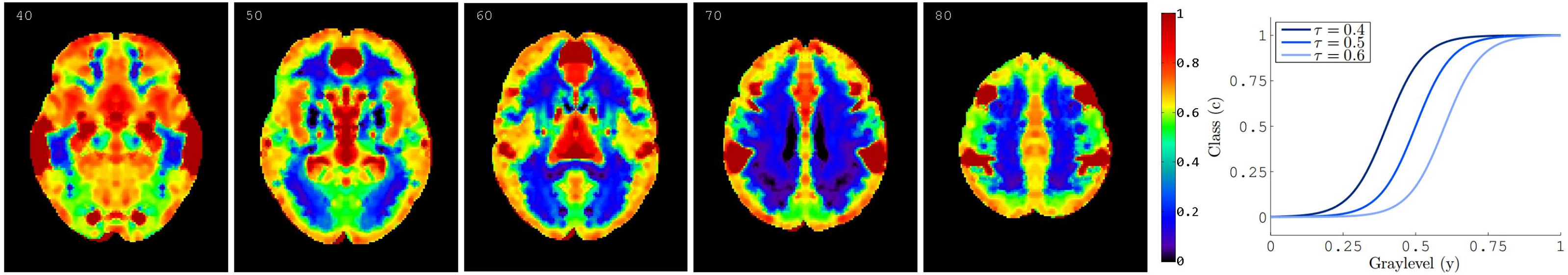
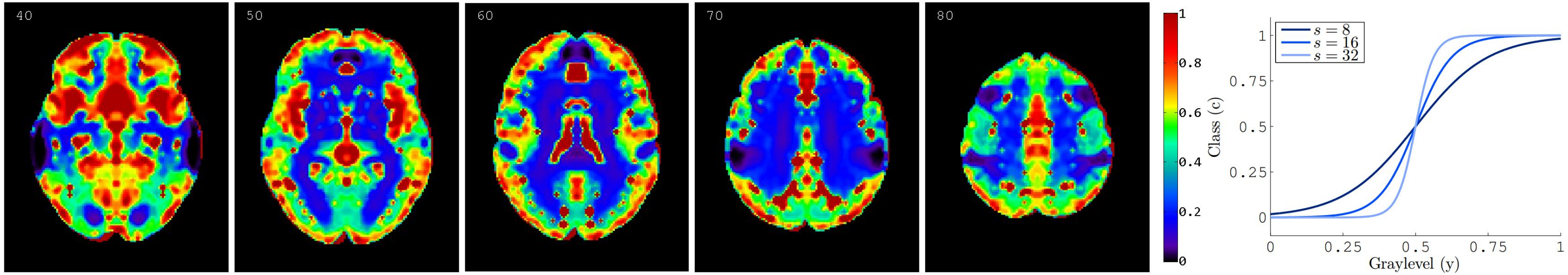
VLR: Parameter Images

$$\eta = \beta_0 + \beta_1 y$$
$$= \mathcal{S}(y - \mathcal{T})$$

$\mathcal{T} = -\beta_0/\beta_1$



$\mathcal{S} = \beta_1$



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VLR: Implementation

Standardization:

- FLAIR intensity $\rightarrow$ histogram matching
- Spatial coordinates $\rightarrow$ MNI space via SPM12

Regularization:

- Data augmentation
  - Reflection & Translation
  - Synthetic Lesions
- MAP estimate: $\boldsymbol{\beta}^* = \arg\max_{\boldsymbol{\beta}} \; \mathcal{L}(\boldsymbol{\beta} \mid \mathcal{C}, \boldsymbol{\mathcal{Y}}) + \lambda ||\boldsymbol{\beta}||_2$

Training Yields:

- One parameter set per voxel $\rightarrow$ One image per parameter

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Segmentation of White Matter Hyperintensities Using Fully Convolutional Network and Transfer Learning

Yongchao Xu [1,2,3], Thierry Géraud [1], Élodie Puybareau [1], Isabelle Bloch [2], Joseph Chazalon [1,4]

[1] EPITA Research and Development Laboratory, France

[2] Télécom ParisTech, Université Paris-Saclay, France

[3] Huazhong University of Science and Technology, China

[4] Université de La Rochelle, France

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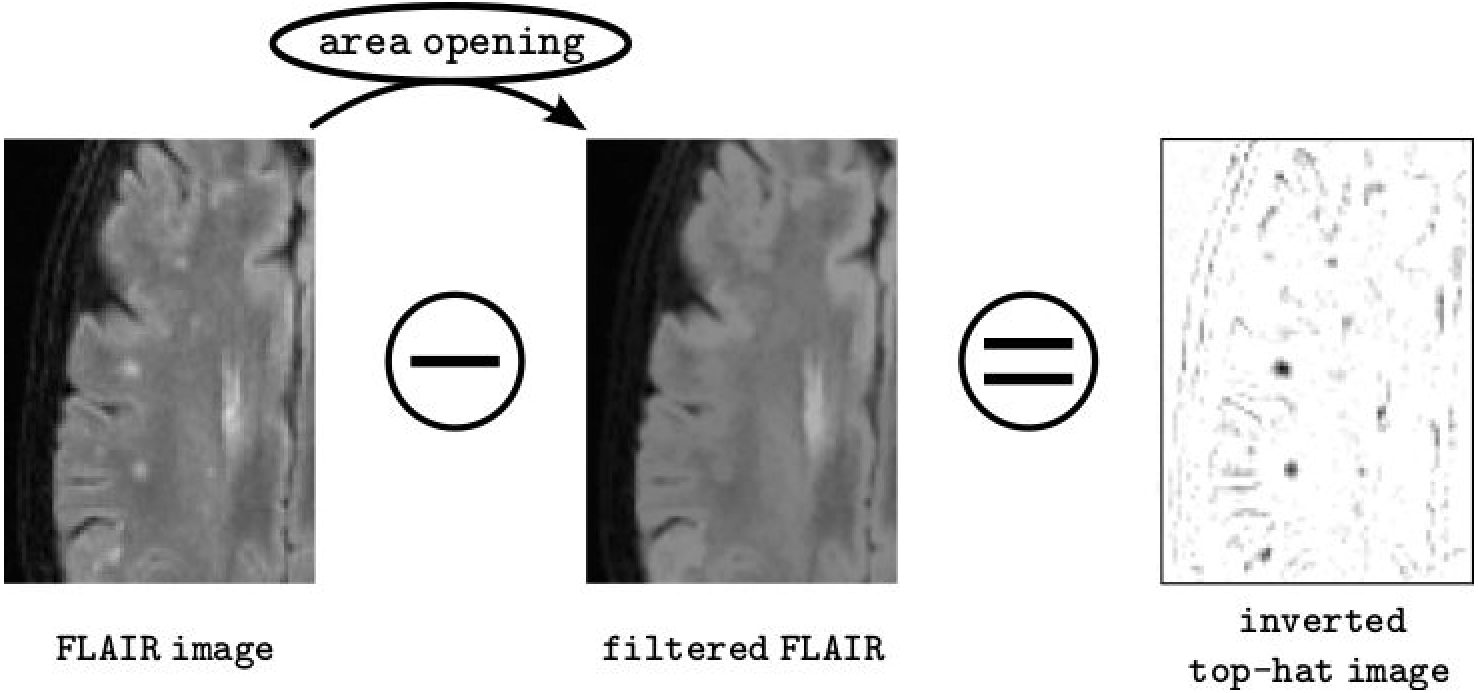
Can we go from small lesions enhancement...



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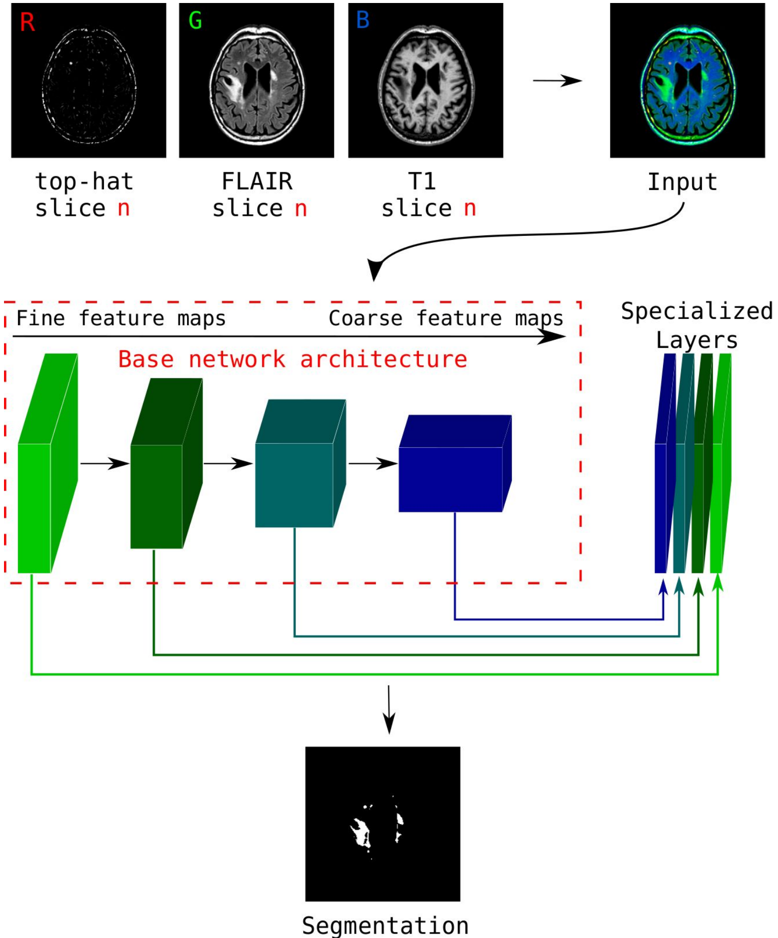
...to WHM segmentation?



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Find the answer at poster **W248**!

Check our **new** article, presented at ICIP 2017:

T. Géraud, Y. Xu, I. Bloch "From Neonatal to Adult Brain MR Image Segmentation in a Few Seconds Using 3D-Like Fully Convolutional Network and Transfer Learning"

http://publications.lrde.epita.fr/xu.17.icip

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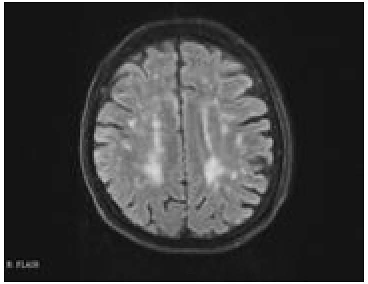
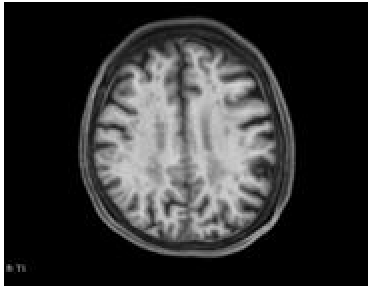
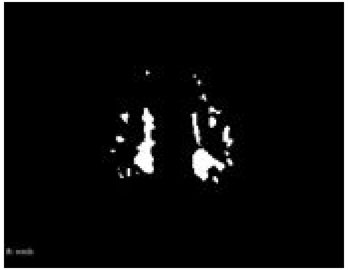
DATA

- Model Input data
  - ../pre/FLAIR.nii.gz
  - ../pre/T1.nii.gz





- Labels
  - ../wmh.nii.gz



- Normalization
  - Image size normalized to 1x1x3 mm spacing (x, y, z respectively)
  - Image intensity normalized from 0 to 1

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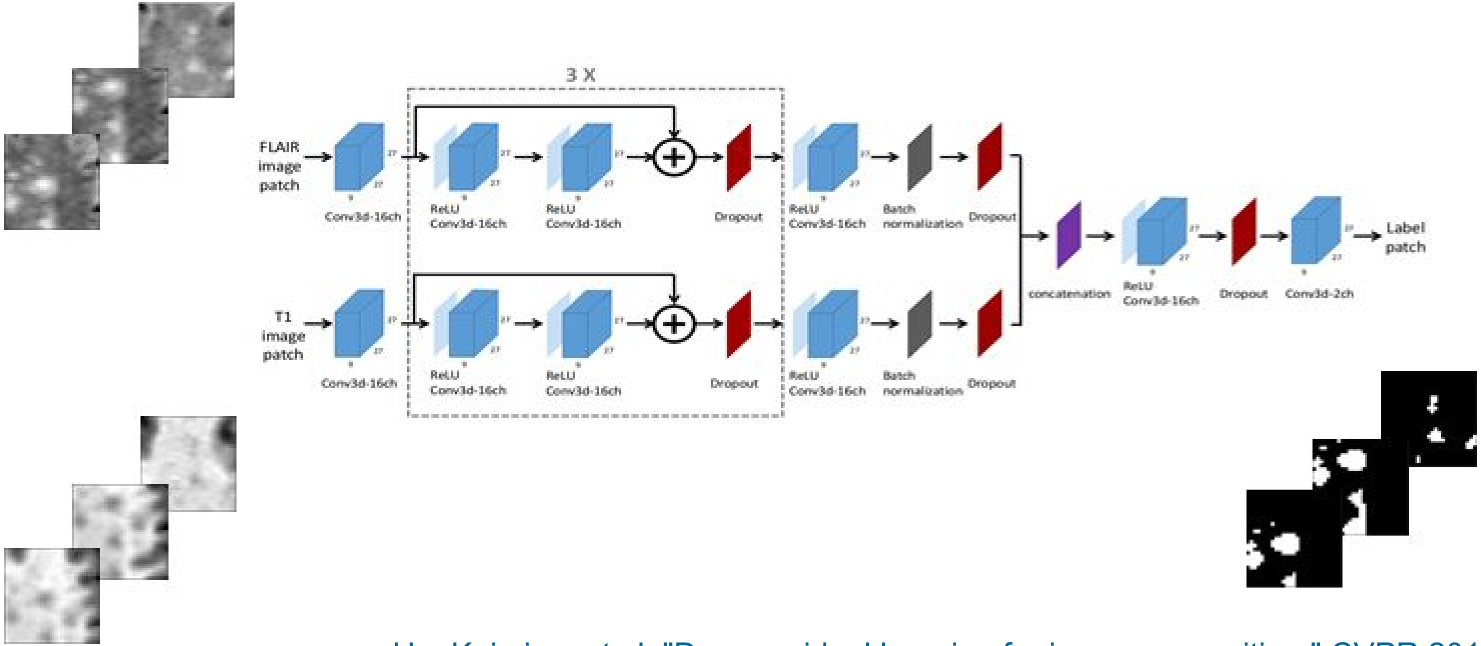
3D CNN WITH SKIP CONNECTIONS



He, Kaiming, et al. "Deep residual learning for image recognition." CVPR 2016.

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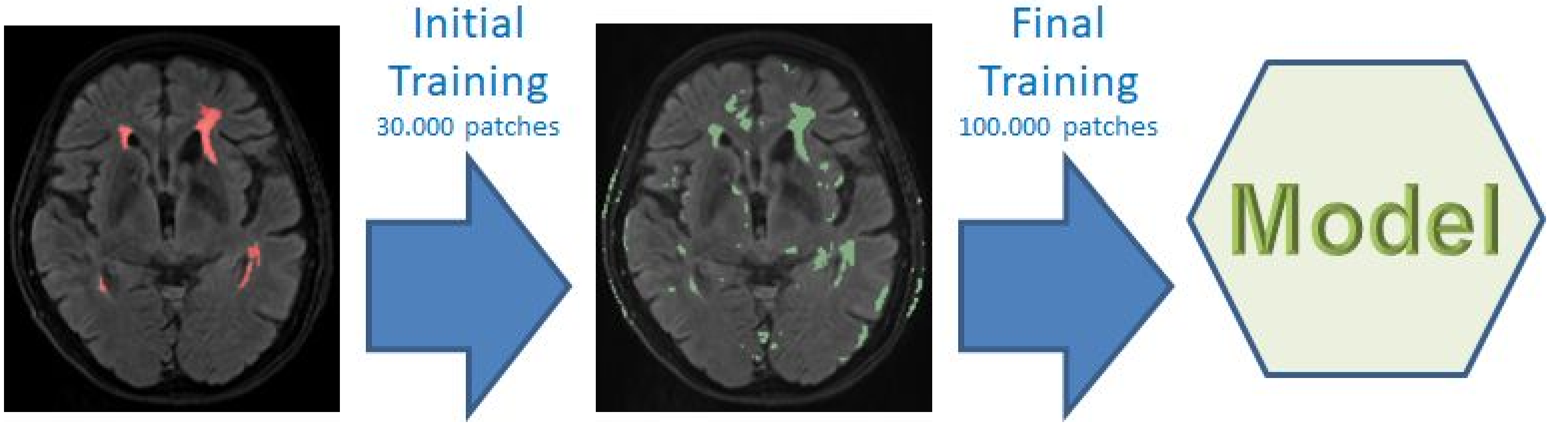
TRAINING



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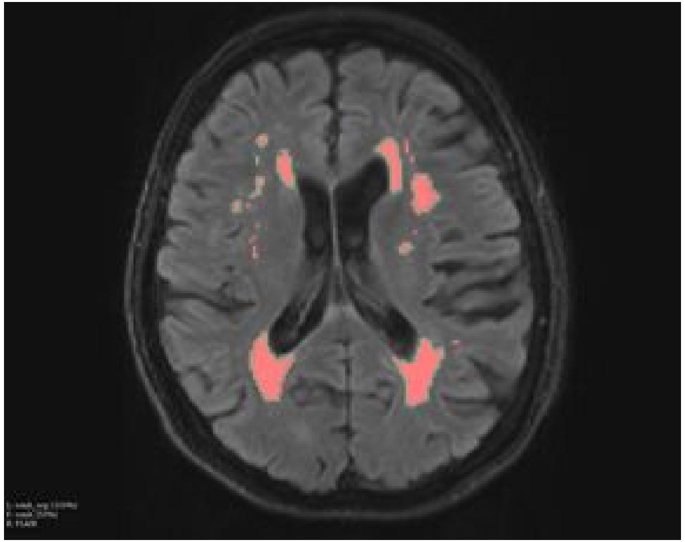
SAMPLING AND RECONSTRUCTION

- Sampling:
  - Patches of 27x27x9 voxels
  - Step size of 9, 9, 3
- Reconstruction:
  - Result patches have 2 channels
  - Sum all patches in a single array
  - Select the highest score per class



Red: Ground truth

Green line: Our result

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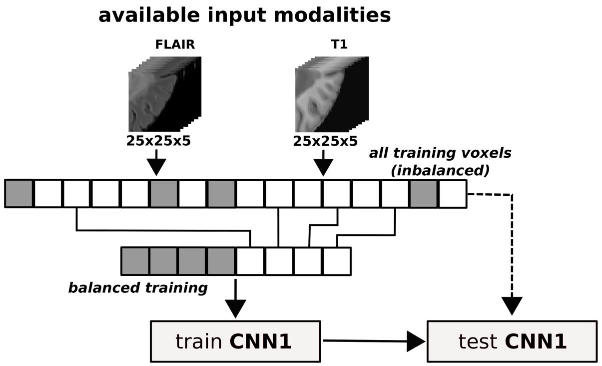
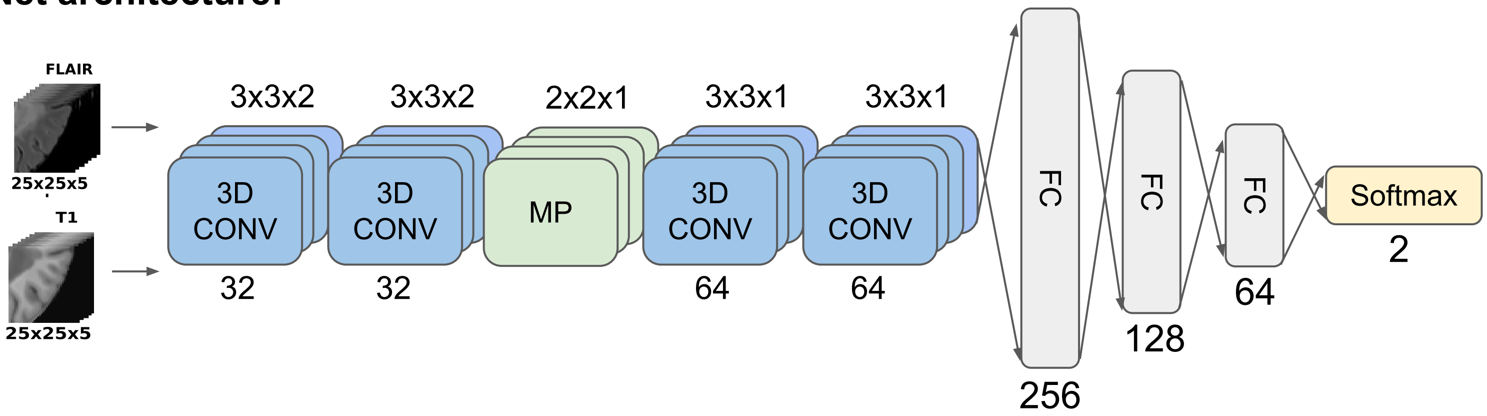
WMH segmentation using a cascade of three CNN



First net (CNN1):

- FLAIR + T1 3D patches (25x25x5)
- Balanced training
  - All positive voxels
  - Same number of randomly selected negatives

Net architecture:



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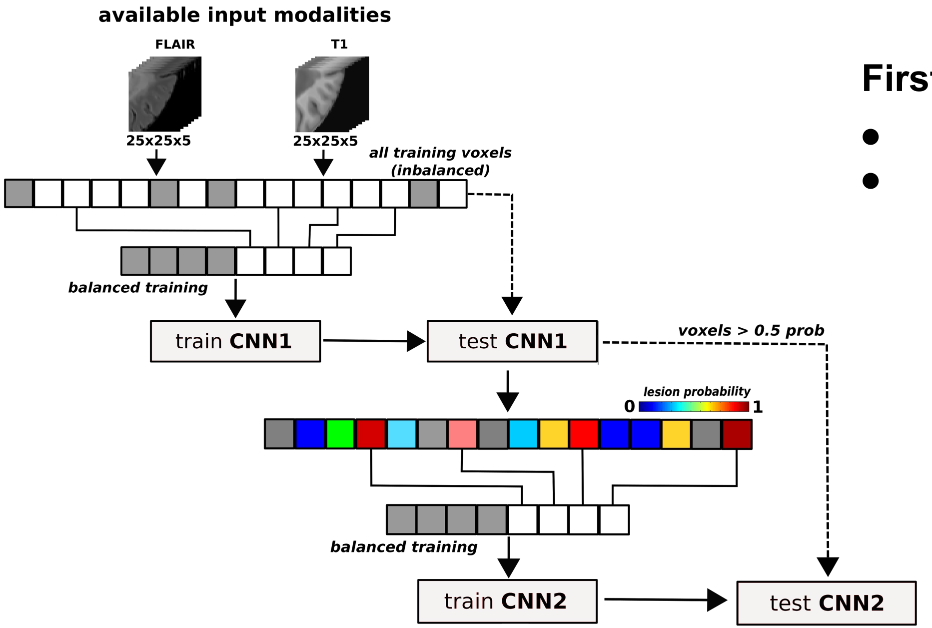

First net (CNN1):

- FLAIR + T1 3D patches (25x25x5)
- Balanced training
  - All positive voxels
  - Same number of randomly selected negatives

Second net (CNN2):

- Balanced training
  - All positive voxels
  - **FP from CNN1 are used to sample negatives** [1]

[1] Valverde, S., Cabezas, M., Roura, E., González-Villà, S., Pareto, D., Vilanova, J. C., … Lladó, X. (2017). Improving automated multiple sclerosis lesion segmentation with a cascaded 3D convolutional neural network approach. *NeuroImage*, *155*, 159–168. https://doi.org/10.1016/j.neuroimage.2017.04.034

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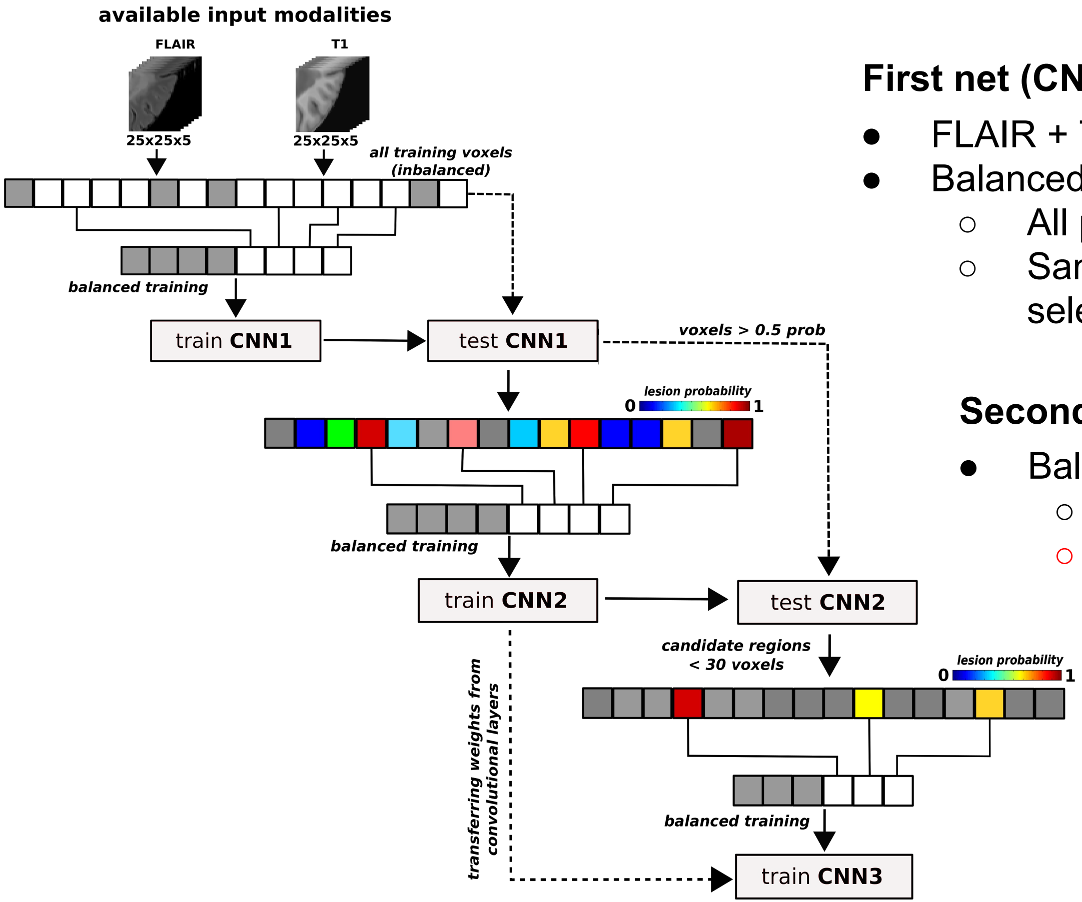
WMH segmentation using a cascade of three CNN



First net (CNN1):

- FLAIR + T1 3D patches (25x25x5)
- Balanced training
  - All positive voxels
  - Same number of randomly selected negatives

Second net (CNN2):

- Balanced training
  - All positive voxels
  - **FP from CNN1 are used to sample negatives**

Third net (CNN3):

- Candidate regions < 30
- Balanced training
- Fine-tuning of CNN2 *(Transfer learning)*

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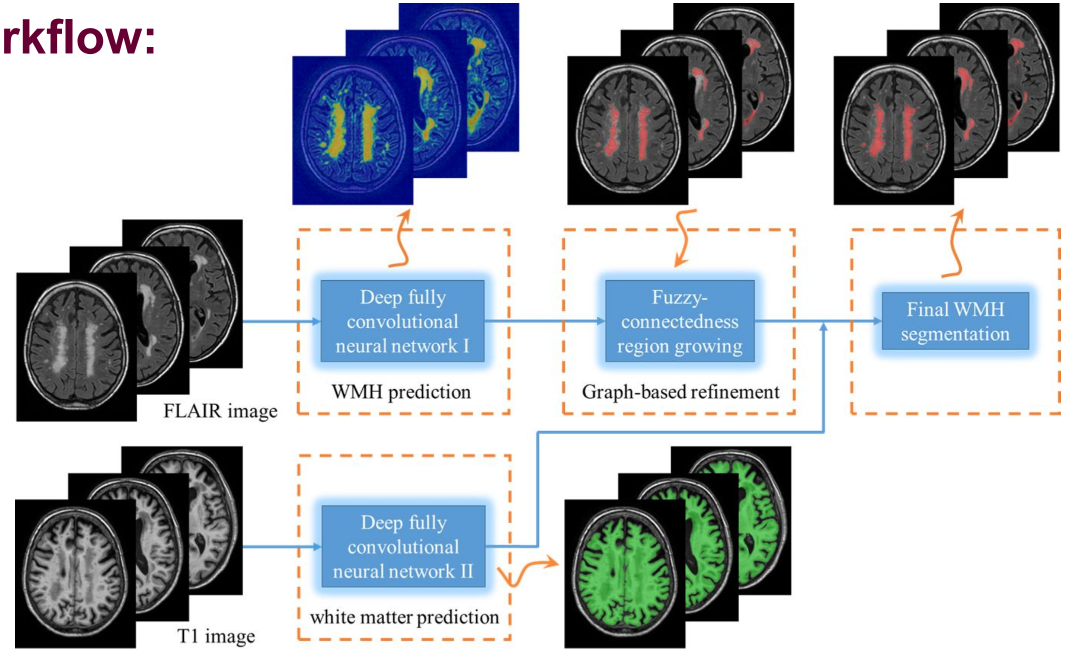
WMH segmentation by deep fully convolutional network and Graph Refinement

Aim: develop a robust deep learning-based WMH segmentation that achieves sufficient sensitivity while greatly reducing false positives

Overall workflow:



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Deep fully convolutional network (FCN) architecture

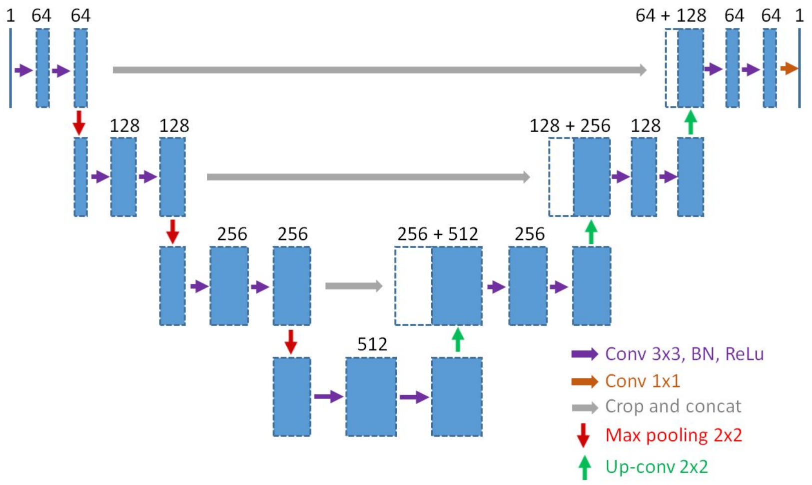
Key Observations for Learning:

- Multiscale anatomy segmentation -> Deep fully convolutional network
- Very small-scale structures -> Relative shallower U-Net architecture
- Unbalanced object and background -> Global weighted loss function
- Inter-subject variability of FCN predictions -> Graph-based post-refinement

FCN Architecture:

- Customized 2D U-Net
- Global weighted loss function to balances WMH & non-WMH

$$loss = -\beta \sum_{j \in Y_+} \log \hat{y}_j - (1-\beta) \sum_{j \in Y_-} \log(1-\hat{y}_j)$$



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Graph-based segmentation refinement

Purpose: Recover the complete WMH regions from high confident FCN predictions with coarse spatial resolutions

Fuzzy connectedness region growing

- ❏ Seed points: high thresholded (>0.97) FCN probability map
- ❏ Fuzzy affinity function combines FCN map and FLAIR intensities:

$$\mu_\kappa(p,q) = \gamma\mu_\kappa\big(FCN(p), FCN(q)\big) + (1-\gamma)\mu_\kappa\big(I(p), I(q)\big), \text{where } \kappa \in \{\psi, \phi\}$$

Note: more weight to FLAIR intensities (γ = 0.25)

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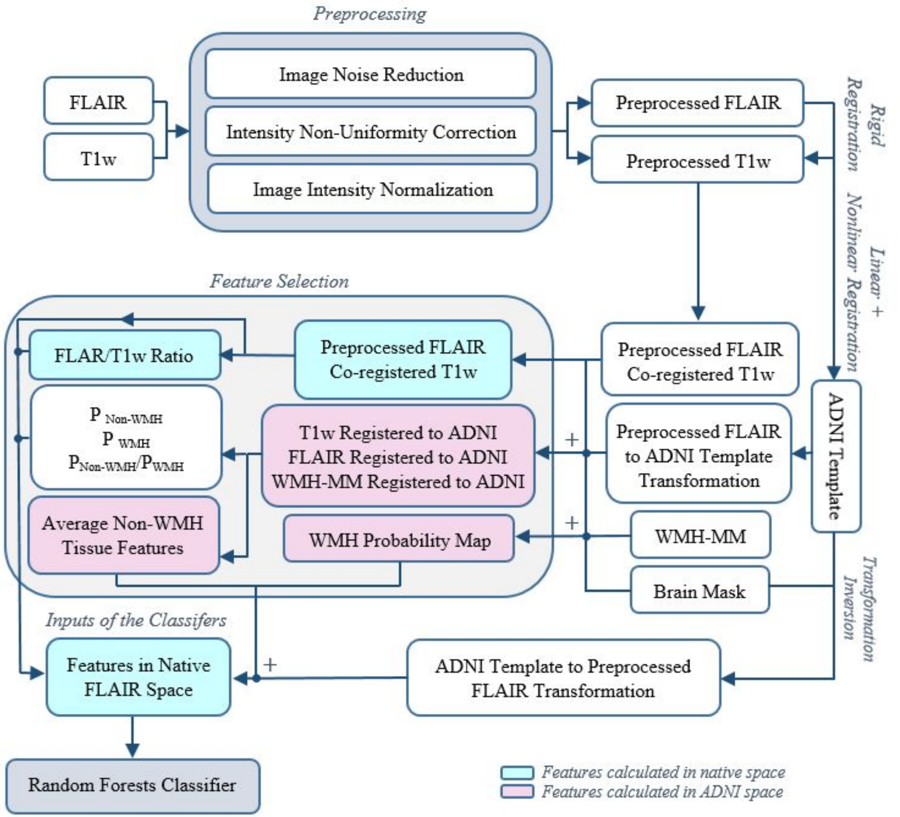
Random Forests Multi-Modal WMH Segmentation Pipeline

NeuroImaging & Surgical Technologies Lab

- Pipeline flow chart:
  - Preprocessing native images
  - Calculating intensity and location features in ADNI template space
  - Transferring features back to native space
  - Random Forests classification
- Segmentations performed in native FLAIR space
- No tissue mask



Dadar et al. "Performance comparison of 10 different classification techniques in segmenting white matter hyperintensities in aging." *NeuroImage* 157 (2017): 233-249.

Dadar et al. "Validation of a Regression Technique for Segmentation of White Matter Hyperintensities in Alzheimer's Disease." *IEEE Transactions on Medical Imaging* (2017).

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Multi-Scale Deep Network, Annealed Training

Preprocessing

1. Brain extracted, remaining pixels scaled between 0.0 and 1.0 (per scan)
2. 32x32, 64x64 and 128x128 patches extracted from all brain pixels
3. Patch = positive if middle pixel overlaps the WMH mask

Architecture

1. Patch based architecture, patches extracted of sizes 32x32, 64x64 and 128x128 for each brain pixel
2. Deep convolutional network (5 conv. layers for each scale). Fusion layers before output layer

Training

1. Adam optimizer, initialized to 1e-2, annealed through 2 epochs of training then reset. Trained for 30 epochs
2. Minibatch of size 768 (128 positive and negative from each of the different sites)

Other Paths

1. No spatial features incorporated
2. No fine-tuning post processing, tried didn't seem to improve
3. Slices independent of neighboring slices

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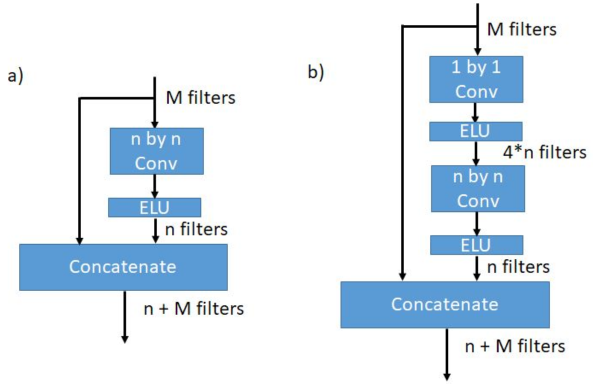
DeepSCAN-WMH: skull-stripping and wmh segmentation with a densely connected deep CNN

- Two-step process: first segment brain, then segment lesions in brain
- Two densely connected fully-convolutional CNNs with no pooling layers



- Ground truth for brain segmentation provided by FSL-FAST

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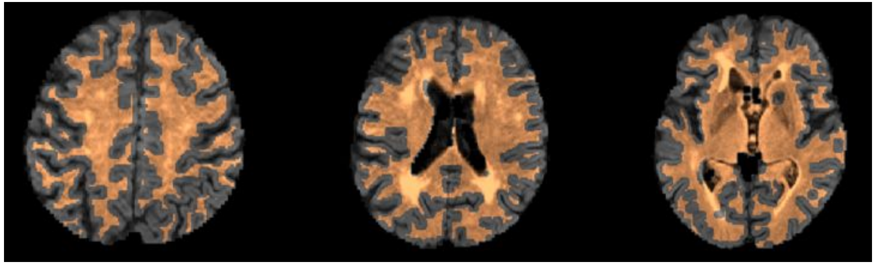
WMH segmentation

MIP Lab. Medical Image Processing

W256 - Team: skkumedneuro

- **{ Preprocessing }** → { Detection } → { Classification }

- Skull stripping (Warping the MNI mask to the data space)
- Segment T1-weighted (GM / WM / CSF)
- Remove CSF partial volume effect map from FLAIR
- Remove skeletonized and dilated CSF mask from FLAIR
- Extract ventricle mask using region growing method
- Remove (dilated ventricle - eroded ventricle) mask from FLAIR
  - Only include the boundary of the ventricle for detecting periventricular WMHs
- Erode the FLAIR mask
- Intensity normalize the FLAIR with mean intensity value of 1,000



FLAIR with final WM mask

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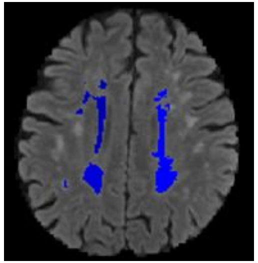
WMH segmentation

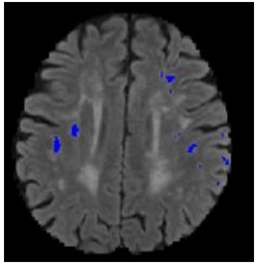
W256 - Team: skkumedneuro

- { Preprocessing } → **{ Detection }** → { Classification }

- **<Periventricular WMHs>**
- Detect the potential WMH voxels: Intensity threshold of mean FLAIR x 1.4
- Make clusters using the detected voxels
- Apply region growing algorithm
  - Seeds: Every voxel in potential WMH clusters with voxel size > 100
  - Stopping intensity threshold: Mean FLAIR x 1.3 (min) ~ Infinite (max)
  - Stopping distance: Maximum 3 mm in Euclidean distance



- **<Deep WMHs>**
- Detect the potential WMH voxels: Intensity threshold of mean FLAIR x 1.3
- Make clusters using the detected voxels
- Apply region growing algorithm
  - Seeds: Every voxel in potential WMH clusters except periventricular WMHs
  - Stopping intensity threshold: Mean FLAIR x 1.3 (min) ~ Infinite (max)
  - Stopping distance: Maximum 3 mm in Euclidean distance
  - Remove the region grown cluster with voxel size > 1,000



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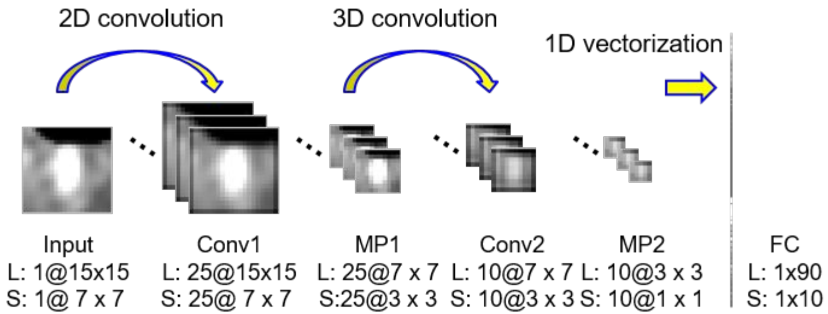
WMH segmentation

W256 - Team: skkumedneuro

- { Preprocessing } → { Detection } → **{ Classification }**

- Intensity normalize T1-weighted and FLAIR
- Extract 239 features
  - 19 texture + 100 multi-layer features from T1-weighted and FLAIR + volume
  - Texture: Max, min, median, mean, variance, energy, standard deviation, root mean square, Range, interquartile range, entropy, uniformity, percentile of 2.5, 25, 50, 75, 97.5
  - Multi-layer: 2 convolutional + 2 max pooling + 1 fully connected layers, patch size of 15 & 7



- Train the random forest model
  - Divide training and test sets (ratio = 8:2)
  - Apply the constructed model to all validation dataset

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Automatic White Matter Hyperintensities Segmentation via U-Net with Two-channel Input

Sun Yat-sen University, China
University of Dundee, Scotland, United Kingdom

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Data Preprocessing

- Selecting slices for training

  The first m slices and last n ones of each patient were removed for a good training set.

- Masking the brain.

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Data Preprocessing

- Each slice was cropped or padded to **200×200**.
- Voxel intensity normalization per patient was performed using **Gaussian Normalization** during the training and testing stage.
- Data augmentation by flipping, rotation, shearing and scaling.

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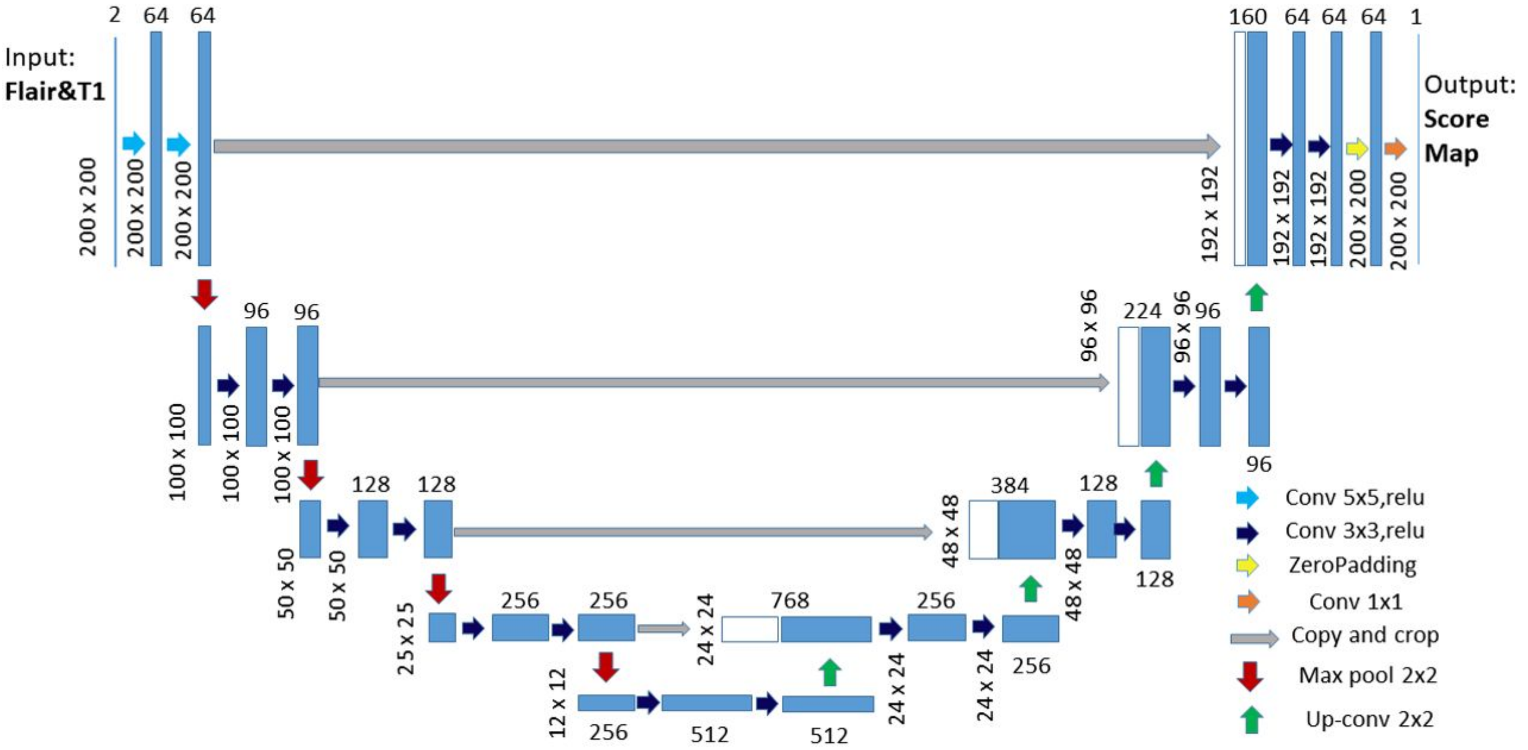
Architecture of Our U-net



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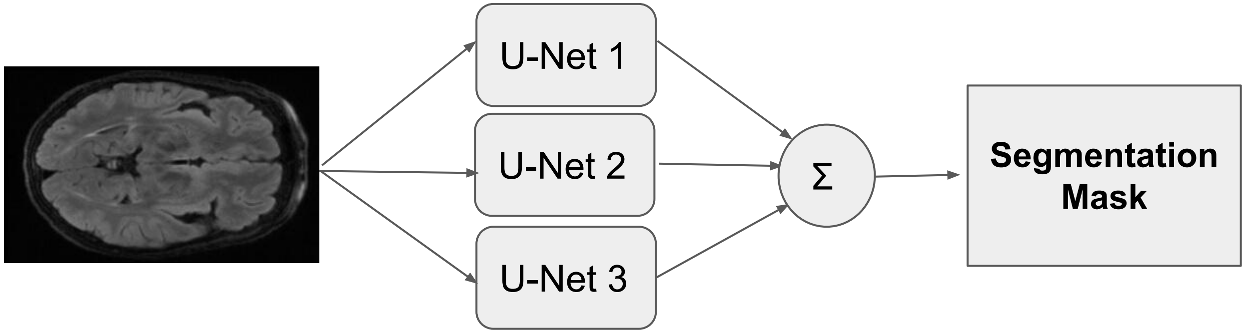
Ensemble Models for Segmentation

- We use three trained U-Net models using same model structures but with different **initializations** through the training process.
- Then we average the scores predicted by the three models.



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Post-processing

One simple strategy

- If there exists predicted WMH in the first ***m*** slices and last ***n*** ones of a brain along the Z-direction, then the WMH regions were considered as false positive and would be removed. m and n were empirically set to **1/8** of number of brain slices of each patient.

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Initial results

80% patients of each training dataset were combined as training set and the rest 20% patients were used as test set.

Initial results on test set:

	Precision	Recall
Utrecht	88.14%	85.29%
Singapore	84.51%	87.42%
Amsterdam-GE3T	78.43%	83.21%

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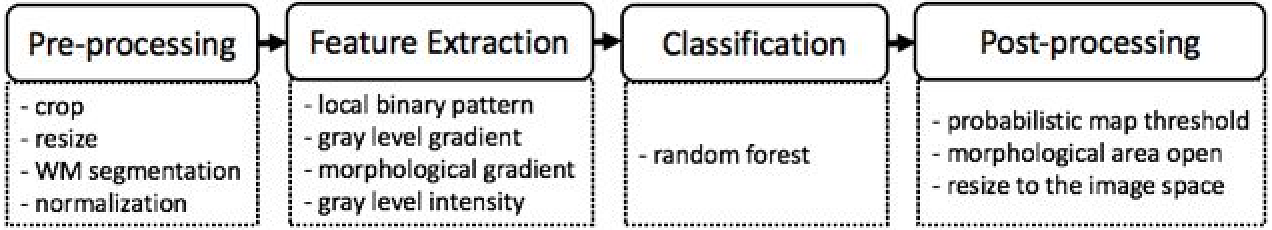
Texture-based Classification Approach

Combine image processing (texture analysis) and pattern recognition (probabilistic classifier)



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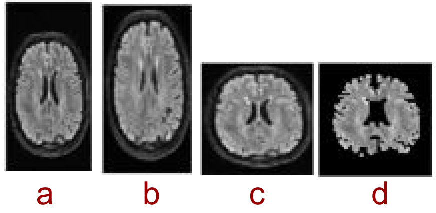
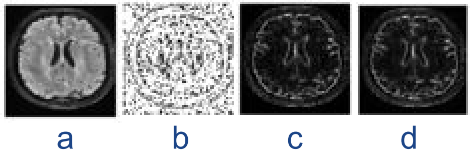
Main steps

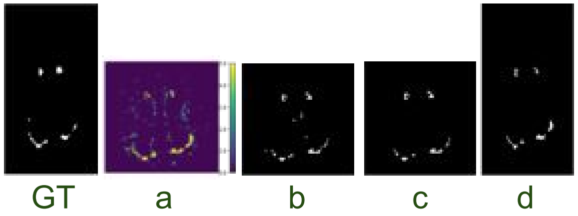
- Pre-processing: original image[a]-> crop[b] -> resize[c] -> wm segmentation[d]



- Feature extraction:
  - T1, FLAIR[a], adjacent FLAIR slices, LBP[b], gradients[c/d] and WM mean intensity (FLAIR)



- Classification: probability of pixel be WMH -> probabilistic map[a]
- Post-processing: thresholding[b]-> area open[c] -> resize to image space[d]



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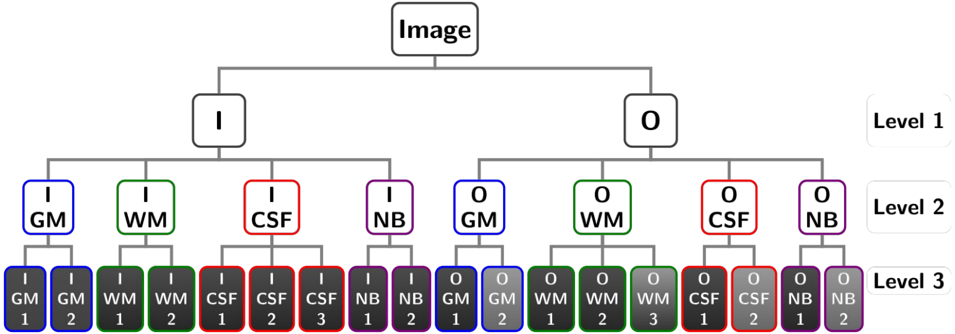
Three-level hierarchical Gaussian mixture model



1. Inlier/Outlier Segmentation - Typicality maps
2. Anatomical tissue - Subject specific prior, Markov Random Field
3. Individual Gaussian components - Inverse Wishart prior over covariance

Model selection:

Split and merge strategy
Acceptance criterion

Post-processing:

Candidate voxel selection

$$L_n = \begin{cases} p_{nO} \cdot \max\left(1, \frac{d_{Mahal}(y_n^{FLAIR})}{3}\right) & \text{if } y_n^{FLAIR} > \mu_{IWM}^{FLAIR} \\ 0 & otherwise \end{cases}$$

Connected component based false positive correction

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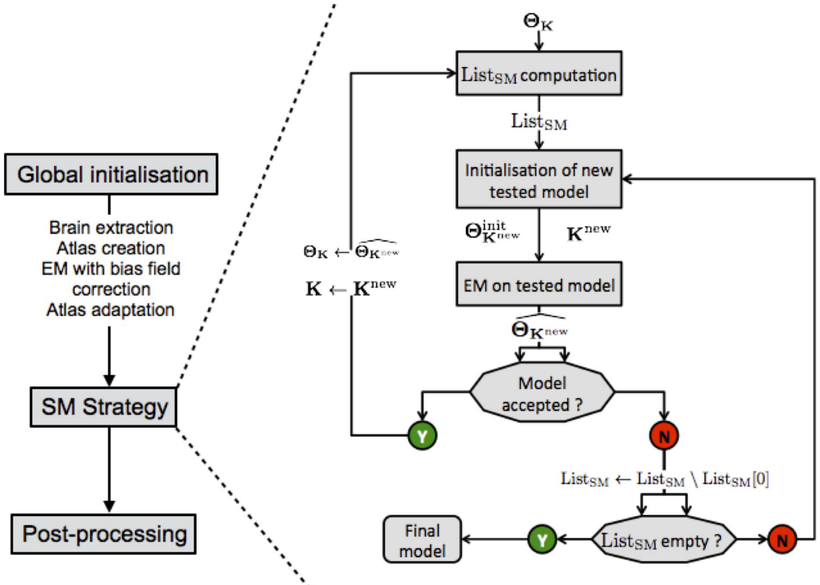
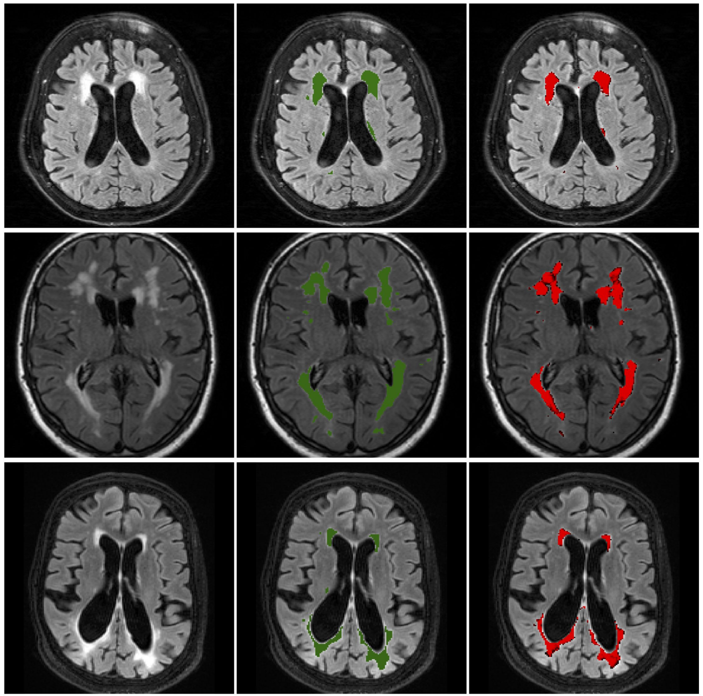
Flowchart



SM Strategy

FLAIR GS BaMoS



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Team TIG Net - Proof of concept NiftyNet

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Training database:

>2500 cases segmented using BaMoS
Variety of scanner types, field strength, manufacturers
Intensity normalisation using piecewise linear transformation

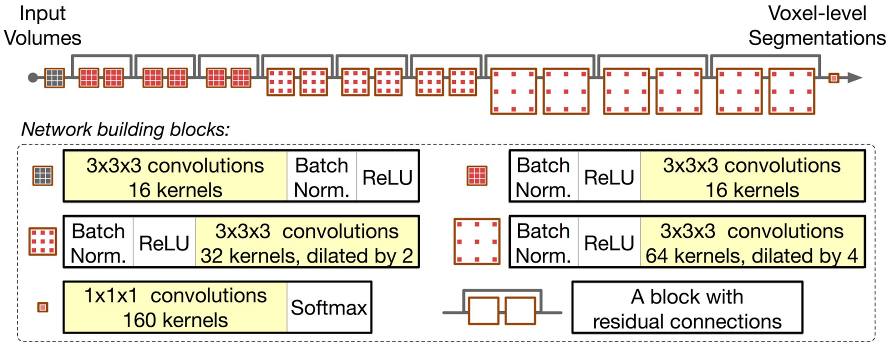
Treatment of class imbalance:

Enforcement of foreground/background ratio
Generalised Dice Loss function

$$\mathrm{GDL} = 1 - 2\frac{\sum_{l=1}^{2} w_l \sum_n r_{ln} p_{ln}}{\sum_{l=1}^{2} w_l \sum_n r_{ln} + p_{ln}}$$

Network architecture:

HighResNet:
Dilated convolutions
Residual connections
Feature batch normalisation



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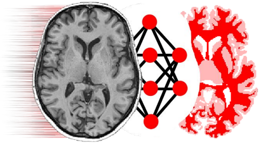
Team TiG Net - Proof of concept NiftyNet

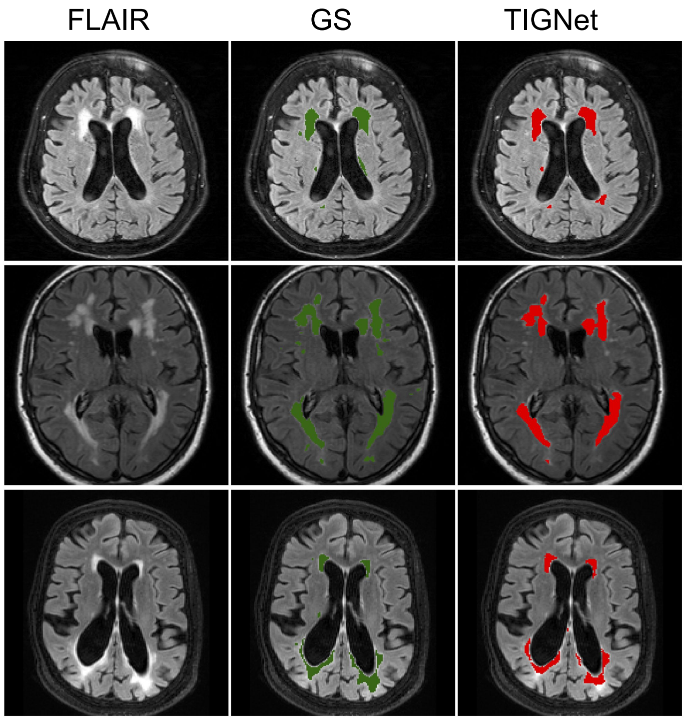
Work in progress:

Adaptive learning schedule
Refinement using manual segmentation
Sampling strategy scheduler



Implementation platform:

www.niftynet.io
Open-source Apache 2 licensed
Tensorflow based
Modular framework
State of the art networks already implemented



Teams:

achilles
cian
hadi
ipmi-bern
k2
knight
lrde
misp
neuro.ml
nic-vicorob
nih_cidi
nist
nlp_logix
scan
skkumedneuro
sysu_media
text_class
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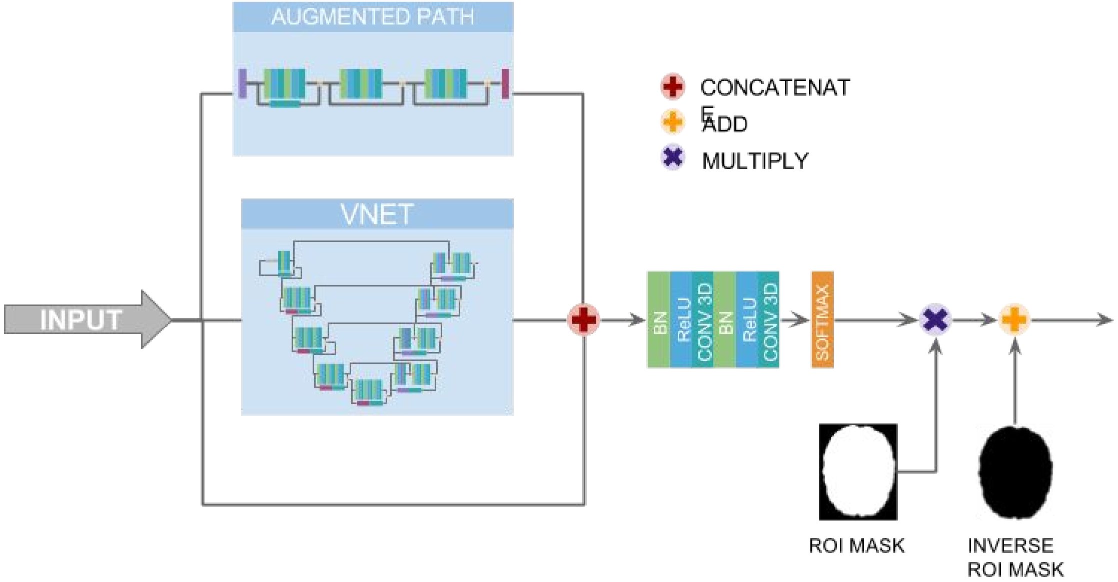
Augmented V-Net: definition



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Augmented V-Net: training & inference

Training:

- Patch-wise training:
  - Train: 32x32x32
  - Fine-tune: 64x64x32, 96x96x32
- Non-uniform sampling:
  - 60% patches are centered in **lesions**, 40% in healthy brain tissue.
- Loss function: cross-entropy (train) and dice (fine-tune)
- Data augmentation: sagittal reflections
- Optimizer: Adam with lr = 0.005

Inference:

- Dense inference, with ROI mask to predict background voxels
- Time: 5-7 seconds per subject

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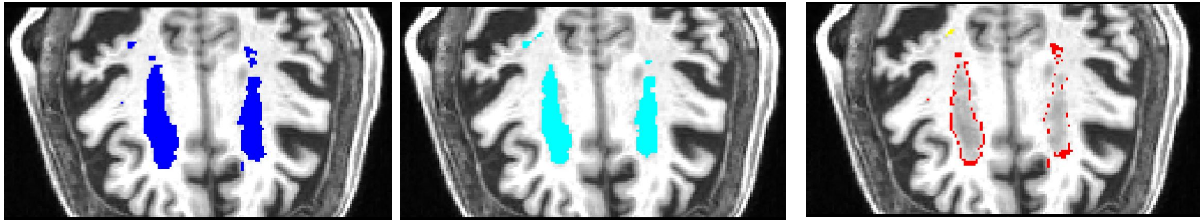
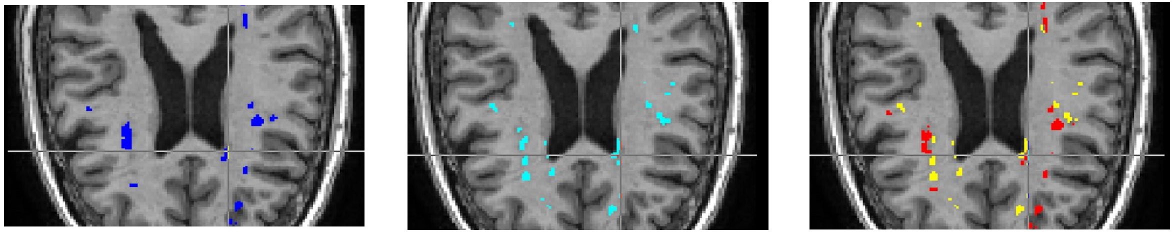
Examples:



Prediction | Ground truth | Difference



Prediction | Ground truth | Difference

Next:

UMC Utrecht

Results, awards, and discussion.