MR Intensity Scale is Arbitrary

- This causes problems in most postprocessing methods
  - Inconsistency or algorithm failure
Problem With Histogram Matching

Image

Target

Subject

Histogram Matched Subject

Histogram
Tissue Classification Result

Image  
Tissue Classified

Original

Histogram Matched

Correct classification

This result yields an underestimation of CSF
MRI Has Multiple Tissue Contrasts

• Uses:
  – Ideal for visualization of certain anomalies
  – Helps in intersubject registration

• Problems:
  – A pulse sequence/image contrast can be missing
  – Desired image can be corrupted or have low resolution
Joint Histogram

$T_2^w$-MPRAGE Joint Histogram (Log color scale)

3 T T2w

3 T MPRAGE
Image Synthesis Framework

Find patches in the atlas image that match that patch

Consider an image patch in the source image

(b) best matches

Atlas T1

Find the patches in the same positions as the best matches

Atlas T2

(c) indexed best matches

Find the patches in the same positions as the best matches

Synthetic T2

(d) combined best matches

= Combine these patches and retain the central pixel

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MIMECS SYNTHESIS METHOD

MR IMage Examplar-based Contrast Synthesis
MIMECS and Sparsity

- Choose one patch?
  - Probably not quite a good match to the subject
- Combine many patches?
  - Any one (bad) patch can spoil the combination
- It is best to use sparsity:
  - Find a small number of patches that will reconstruct the subject patch
  - Use the same coefficients to reconstruct the synthetic patch
The MIMECS Atlas

An overcomplete patch dictionary

Subject Target

\[
A = \{a_1, a_2, \ldots, a_n, a_{n+1}\}
\]

\[
f(i) = [a_1(i)^T \ldots a_n(i)^T]^T
\]

\[
A_1 = [f(1) \ldots f(N)]
\]

\[
A_2 = [\ldots a_{n+1}(i)^T \ldots]
\]
The MIMECS Algorithm

\[ \mathbf{b}_1(j) \approx A_1 \mathbf{x}(j) \]

**B** Subject Images \( \{s_1, s_2, \ldots, s_n\} \)

\[ \mathbf{b}_1(j) = [s_1(j)^T \ldots s_n(j)^T]^T \]

**C**

**D** Synthetic Image \( \hat{s}_{n+1} \)

\[ \hat{\mathbf{b}}_2(j) = A_2 \mathbf{x}(j) \]
Sparse Reconstruction

\[ \mathbf{C} \mathbf{b}_1(j) \approx A_1 \mathbf{x}(j) \]

- The reconstruction should closely match the subject patch \( \mathbf{b}_1(j) \)
- The coefficients in \( \mathbf{x}(j) \) should be sparse
- L2-L1 reconstruction:

\[
\hat{\mathbf{x}}(j) = \arg \min_{\mathbf{x}} \left\{ \| \mathbf{b}_1(j) - A_1 \mathbf{x} \|_2^2 + \lambda \| \mathbf{x} \|_1 \right\}
\]
Reconstruct the Patch in $A_2$

- Reconstruct $A_2$ patch using corresponding patches and the same sparse coefficients

$$\hat{b}_2 = A_2x$$
A Few “Tricks”

- Use kd-tree to reduce the size of $A_1$
  - Use $L_2$ similarity
  - Rapidly finds roughly 100 patches

- We have also explored dictionary learning

- Use +1 higher dimension to normalize patches
  - Dictionary elements should have unit norm
  - If patch dimension = $n-1$
  - Project to sphere in $R^n$
Example 1: Longitudinal Analysis

Single Subject

Original Images

Year 1

Year 4

Year 12

Year 13

Scanner and pulse sequence switched from 1.5T SPGR to 3.0T MPRAGE

Synthetic Images
Example 1: Longitudinal Analysis

GM Volume

Volume (mm$^3$)

Age, years

- SPGR
- Synthetic SPGR
- MPRAGE
- Original SPGR + Synthetic SPGR
Example 2: High Res T2 Synthesis

Brainweb atlas. Both images are high-resolution.

Subject SPGR  Subject T2  Nonlocal means superresolution reconstruction  MIMECS synthesized superresolution image
GENESIS SYNTHESIS METHOD

Generative Sub-Image Synthesis
Gaussian Observation Model

• Suppose each subject patch $x_i$ originates from a single atlas patch $y_j$ as a Gaussian random vector

• Let

$$f_{ij} = x_i - y_j$$

• Then

$$p(x_i; y_j, \Sigma_j) = \frac{1}{\sqrt{(2\pi)^n|\Sigma_j|}} \exp \left\{ -\frac{1}{2} f_{ij}^T \Sigma_j^{-1} f_{ij} \right\}$$
Sparsity-2 Model Is Better

• Suppose each subject patch $x_i$ originates from two atlas patches $y_j$ and $y_k$ as a Gaussian random vector.

• Let $t = \{j, k\}$ and

$$f_{it} = x_i - (\alpha_{it}y_j + (1 - \alpha_{it})y_k)$$

• Then

$$p(x_i; y_j, y_k, \Sigma_t, \alpha_{it}) = \frac{1}{\sqrt{(2\pi)^n|\Sigma_t|}} \exp \left\{ -\frac{1}{2} f_{it}^T \Sigma_t^{-1} f_{it} \right\}$$
What about the Second Modality?

- Assume the same convex combination
  \[ g_{it} = u_i - (\alpha_{it} v_j + (1 - \alpha_{it}) v_k) \]
- Assume independence

\[
p(f, g, z | \Theta) = K \prod_{t \in \Psi} \prod_{i=1}^{N} \left[ \frac{1}{\sigma_{1t}\sigma_{2t}} \exp \left\{ - \frac{||f_{it}||^2}{2\sigma_{1t}^2} \right\} \exp \left\{ - \frac{||g_{it}||^2}{2\sigma_{2t}^2} \right\} \right] z_{it}
\]
ML Estimation using EM Algorithm

- EM algorithm iteratively estimates
  \[ \Theta^{(m)} = \{\sigma_{1t}^{(m)}, \sigma_{2t}^{(m)}, \alpha_{it}^{(m)}; i = 1, \ldots, N, \forall t \} \]

- The E-step computes
  \[ w_{it} = E[z_{it} | f, g, \Theta^{(m)}] \]

- The M-step maximizes likelihood w.r.t. \( \Theta \)

- Patches are synthesized using
  \[ \hat{u}_i = E[u_i | \Theta^{(m)}] = \sum_{t \in \Psi} w_{it}^{(m)} \left( \alpha_{it}^{(m)} v_j + (1 - \alpha_{it}^{(m)}) v_k \right) \]

- They are linear combination of small number of atlas patches
Experiment 3: Intensity Normalization

Subject (\(\alpha = 20^\circ\))

Normalized to \(\alpha = 30^\circ\)

SPGR images with different tip angles

Histograms

\(\alpha=20^\circ\)

\(\alpha=30^\circ\)

Normalized
Experiment 4: MR to CT Image Synthesis

• CT is needed for
  – Surgical planning
  – PET reconstruction

• Sometimes not acquired
  – Avoid dose
  – Not standard of care
  – PET/MR scanners

• Acquire two ultrashort TE MR (UTE) scans; atlas also has CT

• Compared to other methods, GENESIS is far superior
REPLICA SYNTHESIS METHOD

Regression Ensembles with Patch Learning for Image Contrast Agreement
Replica Uses a Regression Framework

Feature vector at $\mathbf{x}$: $\mathbf{f}(\mathbf{x})$

Image value at $\mathbf{x}$: $\mathbf{a}(\mathbf{x})$

Given a training atlas
learn $\mathcal{A}$ such that:

$$\mathbf{a}(\mathbf{x}) \approx \mathcal{A}\{\mathbf{f}(\mathbf{x})\}$$
Building a Single Regression Tree

Let \( f_i = f(x_i) \quad a_i = a(x_i) \)

Training samples at node q:
\( \{(f_1, a_1), (f_2, a_2), \ldots (f_m, a_m)\} \)

Yes

No

Node q:
\( f(k) < \tau \)

\( \bar{a}_q = \frac{1}{m} \sum_{i=1}^{m} a_i \)

\( SSD_q = \sum_{i=1}^{m} (a_i - \bar{a}_q)^2 \)

Choose k and \( \tau \) to minimize
\( SSD_{q_L} + SSD_{q_R} \)

Training samples:
all \( (f_i, a_i) \) s.t. \( f_i(k) < \tau \)

Training samples:
all \( (f_i, a_i) \) s.t. \( f_i(k) \geq \tau \)

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How to Create a Random Forest

• Train 60 regression trees:
  • At each nodal split, consider a random one third of the feature elements
  • Minimize the least squares criterion for these features
  • Recursively partition until there are no fewer than 5 training samples remaining in each leaf node
  • Average each leaf node

• To start, each tree uses bootstrapped training data (patches):
  – Training data are \( \sim 10^5 \) patches from 5 subjects
  – Sampled from all patches (with replacement)

• Training time is approximately 20 minutes
How to Use a Random Forest

• Processing subject images
  – White matter peak normalize all images
  – Form patches and append into feature vectors

• Subject patches
  – Apply to each tree
  – Trace through each tree until hits leaf node
  – Average all leaf nodes to create synthetic image value

• Synthesis takes approximately 1 minute
Patch + Context + Multiscale Features

• Coarse-to-fine process:
  – Synthesize at coarsest level
  – Upsample
  – At next finer level, augment features with coarser synthetic value
Experiment 5: Synthetic FLAIR Images

- Subject images include T1w, T2w, PDw
- Atlas images include T1w, T2w, PDw

True FLAIR

Synthetic FLAIR
Synthetic FLAIR: Saving a “Bad” Dataset

True FLAIR + Lesion TOADs seg.  Synth. FLAIR + Lesion TOADs seg.
Experiment 6: Synthesis with Skull

• $T_1 \rightarrow T_2$ problematic due to intensity ambiguity

• $T_1$-$T_2$ Histogram:
Experiment 6: T2 Synthesis with Skull

- Context features and multiscale are critical
Experiment 7: Intrasubject Registration

**Intra**subject T1w $\Rightarrow$ T2-w deformable registration
PSI-CLONE

Pulse sequence information-based contrast learning on neighborhood ensembles
“Chicken and Egg” Problem

- The subject image must “match” an atlas image
  - In not, cannot choose good patches
- How to make subject image “match” the atlas?
  - Use MIMECS, GENESIS, or REPLICA 😊
- But this requires a matching atlas image
  - Uh oh... 😞
PSI-CLONE Framework

• Estimate subject pulse sequence parameters
  – E.g., TR, $\alpha$, TE

• Synthesize a new *atlas* image $a$ using pulse sequence parameters and atlas quantitative maps

• Use REPLICA training phase to learn a regression from $a$ to the desired atlas contrast

• Use REPLICA synthesis process to synthesize a new subject image with the desired contrast
Estimating Pulse Sequence Parameters

• Underlying tissue properties
  \[ \beta(x) = [P_D(x), T_1(x), T_2(x)] \]

• Assume 3 unknown pulse sequence parameters, e.g.,
  \[ \Theta = [T_E, T_R, \alpha] \]

• Imaging equations
  \[ b_i(x) = \Gamma_i(\beta(x); \Theta_i) \]

• Average tissue parameters in CSF, GM, and WM
  \[ \bar{\beta}_C \quad \bar{\beta}_G \quad \bar{\beta}_W \]

• Carry out 3-class classification of brain
  \[ \bar{b}_{iC} = \Gamma_i(\bar{\beta}_C; \Theta_i) \]
  \[ \bar{b}_{iG} = \Gamma_i(\bar{\beta}_G; \Theta_i) \]
  \[ \bar{b}_{iW} = \Gamma_i(\bar{\beta}_W; \Theta_i) \]

• Solve for \( \Theta \)
Experiment 8: BrainWeb Simulation

• Use quantitative maps from brainweb phantom
• Use Brainweb to synthesize a subject image: $b$
• Carry out Psi-CLONE on the subject to get an “atlas” image $a$ with subject tissue contrast
• Result:
Experiment 9: WM Volume Stability

- Normal human imaged weekly on the same scanner for 9 weeks
- Atlas (different subject):
  - MPRAGE (TR=10.3ms, TE=6ms)
  - Quantitative T1, T2, PD
- Run Psi-CLONE to compute normalized MPRAGE images

- Segment MPRAGE images using TOADS
- Compute relative WM volume (w.r.t. ICV)
- Result:

![Graph showing single subject WM volume stability over 9 weeks.](attachment:image.png)
Summary

• Different methods for image synthesis based on patches:
  – MIMECS
  – GENESIS
  – REPLICA
  – Psi-CLONE

• Many potential applications:
  – Improve consistency of classification/segmentation
  – Stabilize longitudinal analysis
  – Generate high resolution alternative contrasts
  – Enhance abnormal features (e.g., lesions)
  – Improve cross modal registration
  – Reduce artifacts
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QUESTIONS?