Summary of *Symmetric diffeomorphic image registration with cross-correlation: Evaluating automated labeling of elderly and neurodegenerative brain*

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1. **Abstract:**

This article developed a novel symmetric image normalization method (SyN) for maximizing the cross-correlation within the space of diffeomorphic maps and provide the Euler–Lagrange equations necessary for this optimization.

Evaluation: gold standard- human cortical segmentation to contrast SyN's performance with a related elastic method and with the standard ITK implementation of Thirion's Demons algorithm.

→ SyN is better especially when the distance between the template brain and the target brain is large

2. **Introduction:**

Problem:

(1) MRI studies of individual patients are difficult to interpret because of the wide range of acceptable, age-related atrophy in an older cohort sus- ceptible to dementia.

(2) The manual approach remains, however, severely limited by the complexity of labeling 2563 or more voxels.

(3) The problem of inter-rater variability which limits the reliability of manual labeling

3. **Some methods of registration**

(1) Demons:

- Thirion,1996
- Uses an approximate elastic regularizer to solve an optical flow problem, where the moving image's level sets are brought into correspondence with those of a reference of fixed template image.
- Use Dice statistic to compare:

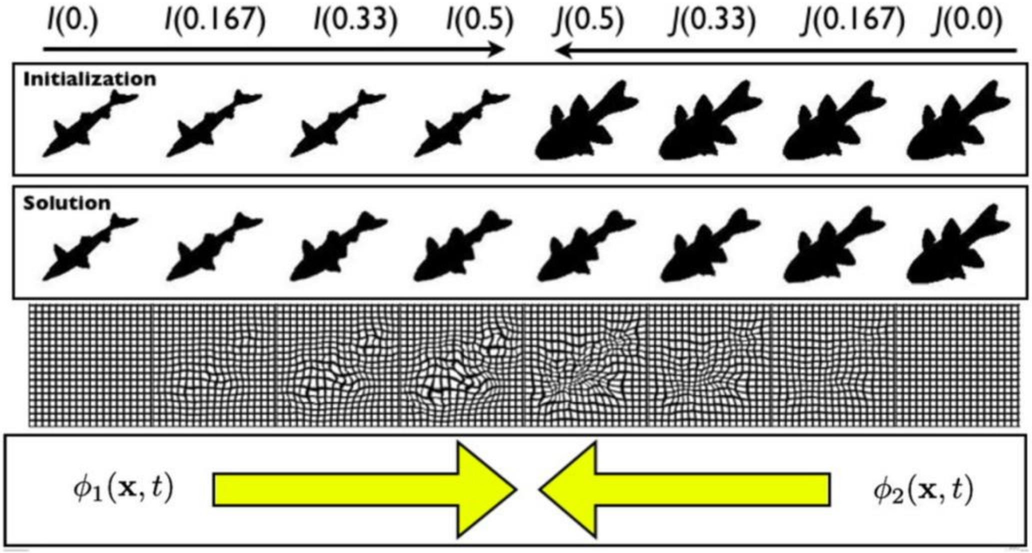
$$S(R1, R2) = \frac{2\sharp(R1 \cap R2)}{\sharp(R1) + \sharp(R2)},$$

Which measures both difference in size and location between two segmentations R1 and R2. The # counts the number of pixels in the region.

(2) Symmetric diffeomorphisms

- Define a diffeomorphism ϕ of domain Ω, for transforming image I into a new coordinate system by $\phi I = I \circ \phi(x, t = 1) = I\big(\phi(x, t = 1)\big)$, which indicates that I is warped forward by the map defined by $\phi(x, 1)$.

- This is a visualization of the components of ϕ.



- The top row are the original images, I and J, the second row is the SyN solution converging outputs. The deforming grids associated with these diffeomorphisms are shown in the bottom row.
- Set time t=0.5, then the forward and backward optimization problem is:

$$E_{\mathrm{sym}}(I,J) = \inf_{\phi_1} \inf_{\phi_2} \int_{t=0}^{0.5} \left\{ \|\boldsymbol{v}_1(\mathbf{x},t)\|_L^2 + \|\boldsymbol{v}_2(\mathbf{x},t)\|_L^2 \right\} \mathrm{d}t + \int_\Omega |I(\phi_1(0.5)) - J(\phi_2(0.5))|^2 \, \mathrm{d}\Omega.$$

Subject to each $\phi_{\mathrm{i}} \in \mathit{Diff}_0$ the solution of:

$$\mathrm{d}\phi_i(\mathbf{x},t)/\mathrm{d}t = \boldsymbol{v}_i(\phi_i(\mathbf{x},t),t) \text{ with } \phi_i(\mathbf{x},0) = \mathbf{Id} \text{ and } \phi_i^{-1}(\phi_i) = \mathbf{Id}, \phi_i(\phi_i^{-1}) = \mathbf{Id}.$$

Forward warp I:

$$\phi I = I \circ \phi(x, t=1) = I(\phi(x, t=1))$$

Backward warp $\phi^{-1}(x, 1)$

- L: the linear differential operator
- t: time
- x: a spatial coordinate
- $v(x, t)$: a velocity field
- ϕ: diffeomorphism
- Ω: domain

$$\phi(x, 1) = \phi(x, 0) + \int_0^1 v(\underbrace{\phi(x, t)}_{y}, t)\, dt$$

$$D(\phi(x, 0), \phi(x, 1)) = \int_0^1 \| v(x, t) \|_L\, dt$$

$$L = a\nabla^2 + b\, Id$$

Facts: $\phi \to \phi_1, \phi_2$

- x : I
- z : J

$$D(Id, \phi_1(x, 0.5)) = D(Id, \phi_2(z, 0.5))$$

Costraint: $D(\phi_1(x, 0.5)) = D(\phi_2(x, 0.5))$

$$\phi_1^{-1}(\phi_1) = Id, \quad \phi_2^{-1}(\phi_2) = Id$$

$$\rightarrow \phi_1(x, 1) = \phi_2^{-1}(\phi_1(x, 0.5), 0.5)$$

(3) The cross-correlation with symmetric diffeomorphisms

Cross-correlation (CC) adapts natu- rally to situations where locally varying intensities occur and is suitable for some multi-modality problems. The CC depends only on estimates of the local image average and variance which may be accurately/exactly measured with relatively few samples. Furthermore, the cross-corre- lation has shown historically to perform well in many real-world computer vision applications where one requires robustness to unpredictable illumination, reflectance, etc.

Example: revisit the classical cross-correlation as a similarity metric for use in our emerging diffeomorphic image registration.

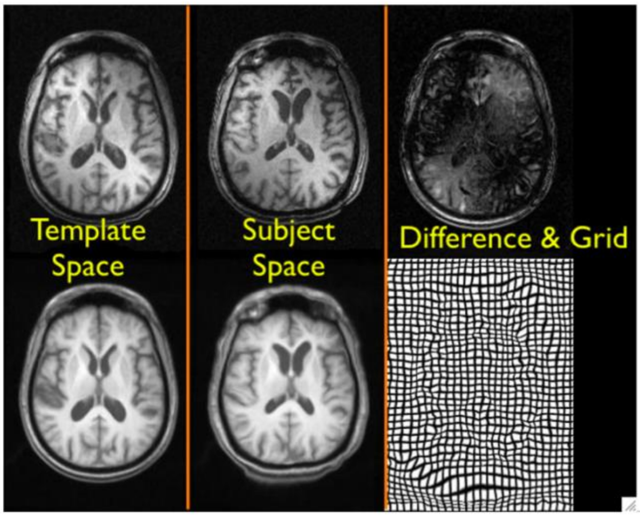


Fig. 3. The local cross-correlation measure allows robust matching of images despite the presence of a strong bias field affecting the image quality. The smoothness of the grid is also unaffected by the bias.

$$E_{CC}(\bar{I},\bar{J}) = \inf_{\phi_1} \inf_{\phi_2} \int_{t=0}^{0.5} \left\{ \|\boldsymbol{v}_1(\mathbf{x},t)\|_L^2 + \|\boldsymbol{v}_2(\mathbf{x},t)\|_L^2 \right\} \mathrm{d}t + \int_{\Omega} CC(\bar{I},\bar{J},\mathbf{x}) \mathrm{d}\Omega.$$

Subject to each $\phi_{\mathrm{i}} \in Diff_0$ the solution of:

$$\mathrm{d}\phi_i(\mathbf{x},t)/\mathrm{d}t = \boldsymbol{v}_i(\phi_i(x,t),t) \text{ with } \phi_i(\mathbf{x},0) = \mathbf{Id} \text{ and } \phi_i^{-1}(\phi_i) = \mathbf{Id}, \phi_i(\phi_i^{-1}) = \mathbf{Id}.$$

$$\nabla_{\phi_1(\mathbf{x},0.5)} E_{CC}(\mathbf{x}), = 2L\mathbf{v}_1(\mathbf{x}, 0.5) + \frac{2A}{BC} \times \left(\bar{J}(\mathbf{x}) - \frac{A}{B}\bar{I}(\mathbf{x})\right) |D\phi_1| \nabla \bar{I}(\mathbf{x}),$$

$$\nabla_{\phi_2(\mathbf{x},0.5)} E_{CC}(\mathbf{x}), = 2L\mathbf{v}_2(\mathbf{x}, 0.5) + \frac{2A}{BC} \times \left(\bar{I}(\mathbf{x}) - \frac{A}{C}\bar{J}(\mathbf{x})\right) |D\phi_2| \nabla \bar{J}(\mathbf{x}).$$

Algorithm 1 (*Computing cross-correlation derivatives*).

(1) Deform I by $\phi_1(0.5)$ and J by $\phi_2(0.5)$.
(2) Calculate $\bar{I}$ and $\bar{J}$ from the result of step (1).
(3) Calculate and store images representing A, B and C.

Algorithm 2

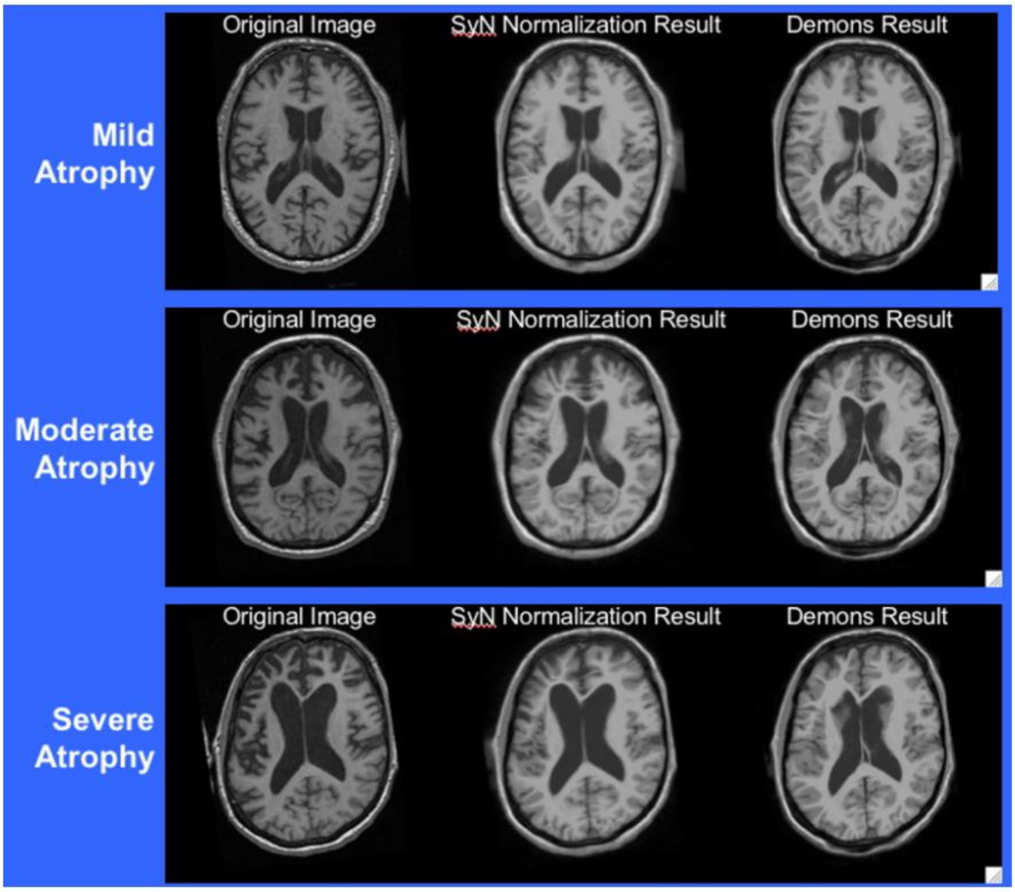
1: **while** $\|\psi^{-1}(\phi(\mathbf{x})) - \mathbf{x}\|_\infty > \epsilon_2 r$ **do**
2: Compute $v^{-1}(\mathbf{x}) = \psi^{-1}(\phi(\mathbf{x})) - \mathbf{x}$.
3: Find scalar γ such that $\|v^{-1}\|_\infty = 0.5r$.
4: Integrate ψ^{-1} s.t. $\psi^{-1}(\tilde{\mathbf{y}}, t) + = \gamma \mathbf{v}^{-1}(\psi^{-1}(\tilde{\mathbf{y}}, t))$.
5: **end while**

Algorithm 3

(1) Initialize $\phi_1 = \mathbf{Id} = \phi_1^{-1}$ and $\phi_2 = \mathbf{Id} = \phi_2^{-1}$.
(2) Repeat the following steps until convergence:

(3) Compute the cross-correlation as described in Algorithm 1.
(4) Compute each v_i by smoothing the result of step (3) in this table. One may also use the modified midpoint method for each velocity, as in the LPF algorithm (Avants et al., 2006a), to give smoothness in time.
(5) Update each ϕ_i by v_i through the *o.d.e.* as described in Eq. (8). This step automatically adjusts the time step-size such that the maximum length of the updates to the ϕ_i is sub-pixel and approximately constant over iterations. We explicitly guarantee $\|\mathbf{v}_1(\cdot, t)\| = \|\mathbf{v}_2(\cdot, t)\|$. We also update the estimate to the geodesic distance by trapezoidal rule, as in the LPF method.

(6) Use Algorithm 2 to get the inverses of the ϕ_i.
(7) Generate the time 1 solutions from $\phi_1(1) = \phi_2^{-1}(\phi_1(\mathbf{x}, 0.5), 0.5)$ and $\phi_1^{-1}(1) = \phi_2(1) = \phi_1^{-1}(\phi_2(\mathbf{x}, 0.5), 0.5)$.



Mild Atrophy
Moderate Atrophy
Severe Atrophy
Original Image
SyN Normalization Result
Demons Result
Original Image
SyN Normalization Result
Demons Result
Original Image
SyN Normalization Result
Demons Result