



Mermaid and Voxelmorph framework for medical image registration

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20.08.2021



Outline

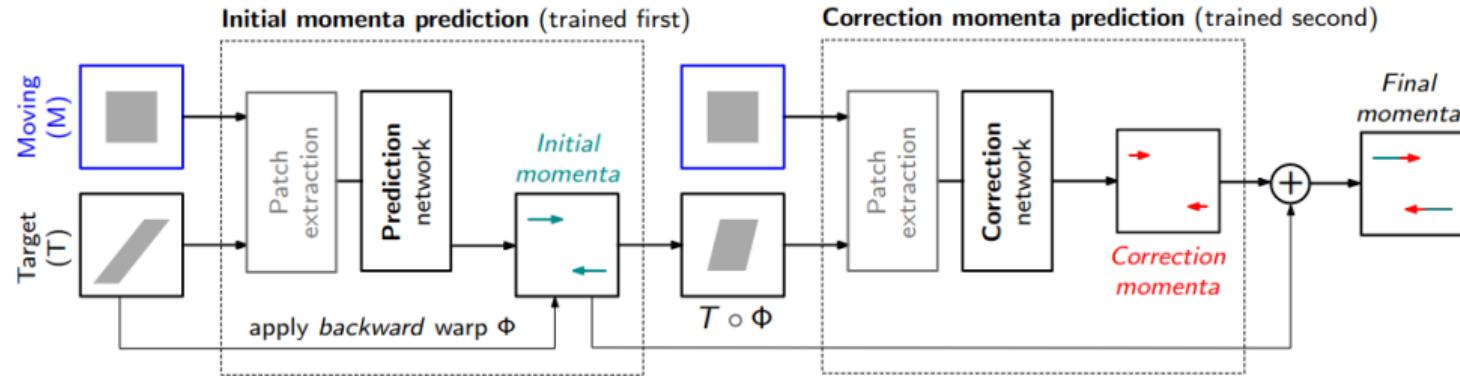
1. Mermaid

2. Voxelmorph

Mermaid

- supervised NN Quicksilver
- spatially varying regularizer
- affine and non-parametric network combined ASVM
- ASVM + spatio-temporal regularizer RDMM

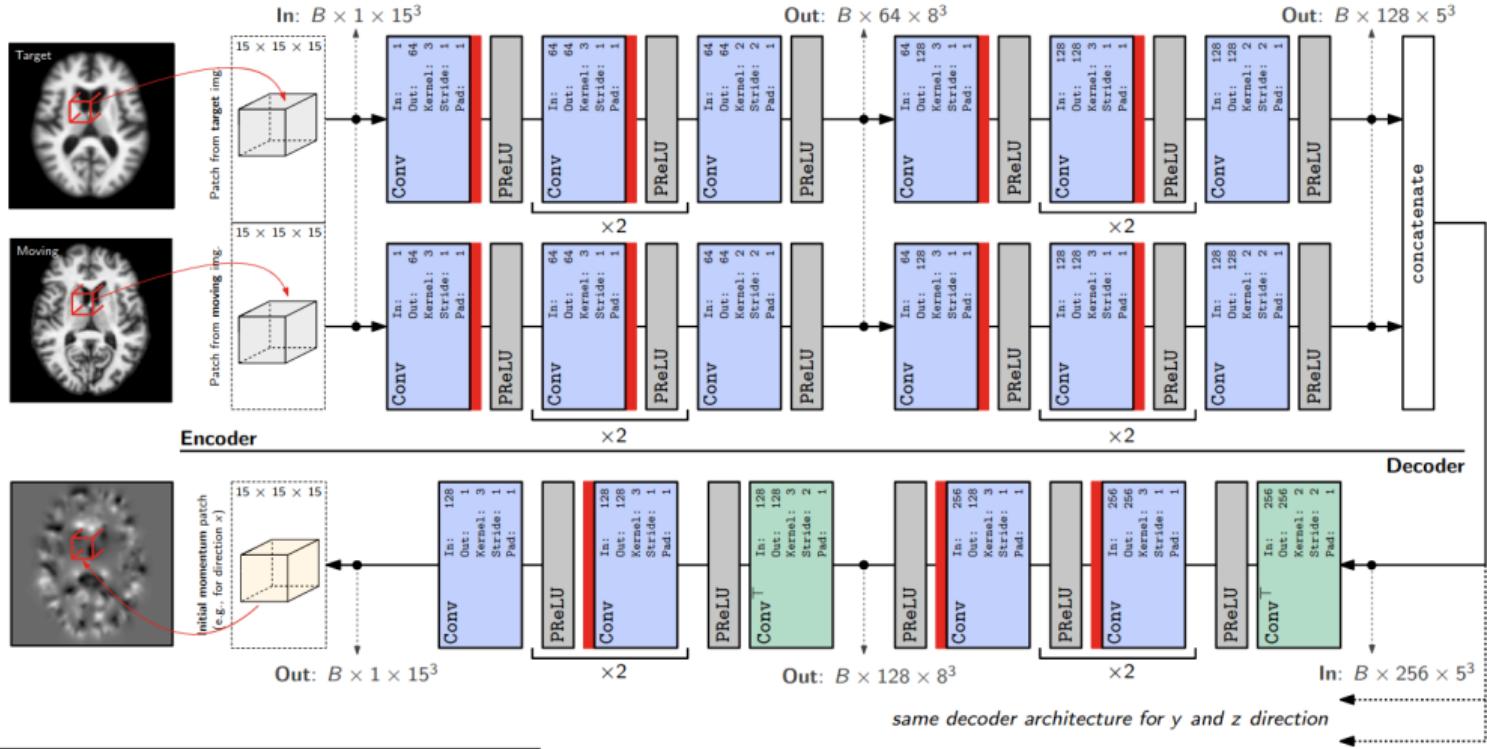
Quicksilver



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¹Xiao Yang et al. 2017. “Quicksilver: Fast predictive image registration—a deep learning approach.” *NeuroImage* 158:378–396.

Quicksilver network architecture



Metric learning

$$v = \left(\sum_{i=0}^{N-1} w_i G_i \right) \star m, \quad w_i > 0, \quad \sum_{i=0}^{N-1} w_i = 1$$

Metric learning

$$v = \left(\sum_{i=0}^{N-1} w_i G_i \right) \star m, \quad w_i > 0, \quad \sum_{i=0}^{N-1} w_i = 1$$

$$\widehat{OMT}(w) = \left| \log \frac{\sigma_{N-1}}{\sigma_0} \right|^{-r} \sum_{i=0}^{N-1} w_i \left| \log \frac{\sigma_{N-1}}{\sigma_i} \right|^r$$

Metric learning

$$v_0(x) = \sum_{i=0}^{N-1} \sqrt{w_i(x)} \int_y G_i(|x - y|) \sqrt{w_i(y)} m_0(y) dy$$

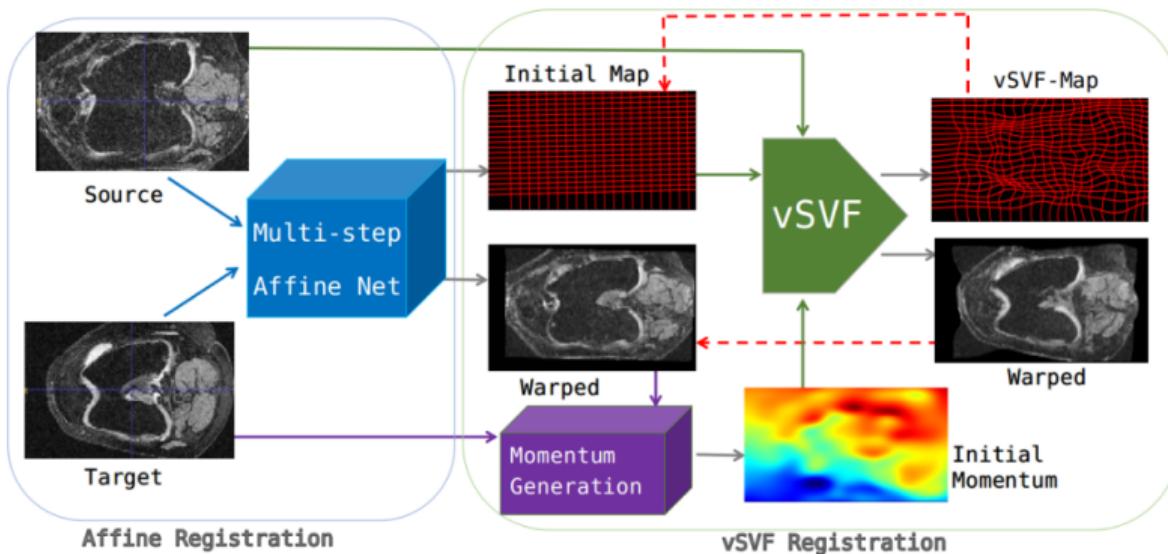
Metric learning

$$v_0(x) = \sum_{i=0}^{N-1} \sqrt{w_i(x)} \int_y G_i(|x-y|) \sqrt{w_i(y)} m_0(y) dy$$
$$w_i(x) = G_{\sigma_{small}} \star \omega_i(x)$$

Metric learning

$conv(d + 1, n_1) \rightarrow BatchNorm \rightarrow lReLU$
 $\rightarrow conv(n_1, N) \rightarrow BatchNorm \rightarrow weighted-linear-softmax$

ASVM - affine-vSVF-Mapping

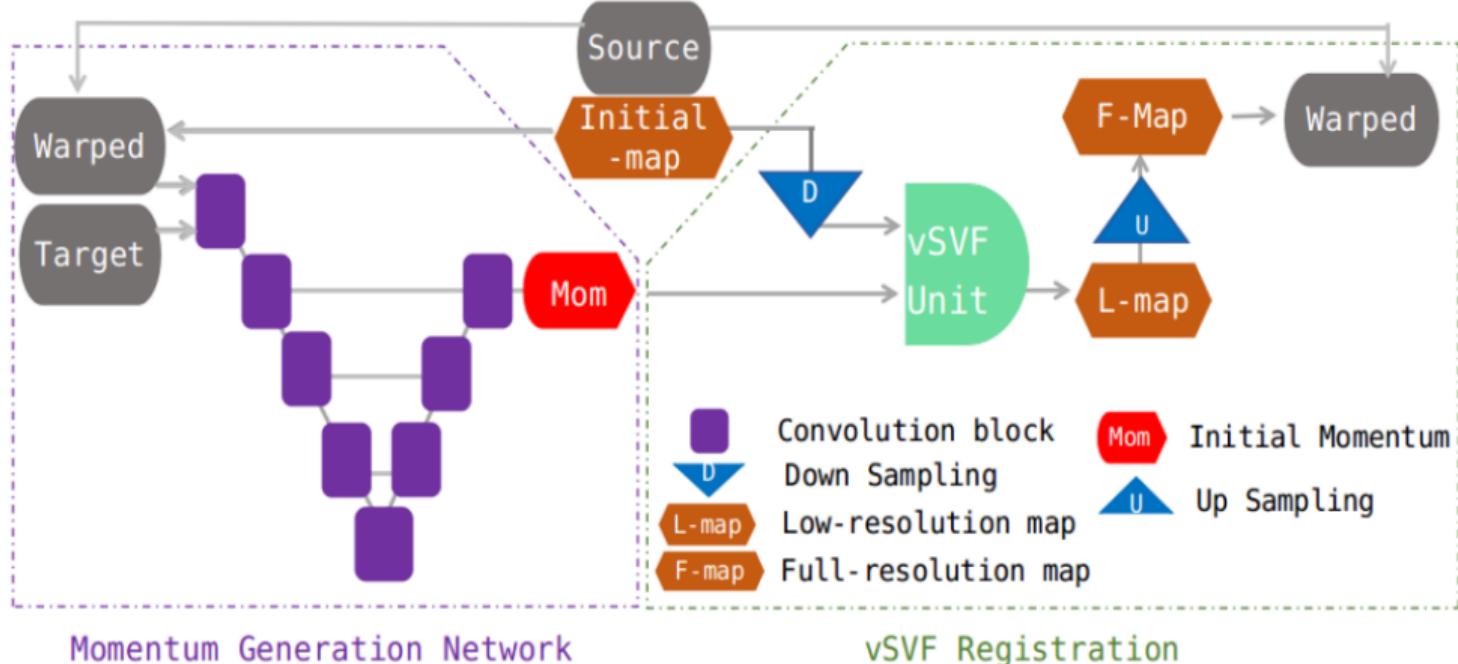


³Zhengyang Shen et al. 2019. “Networks for Joint Affine and Non-parametric Image Registration.” In *Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition*, 4224–4233.

ASVM loss function

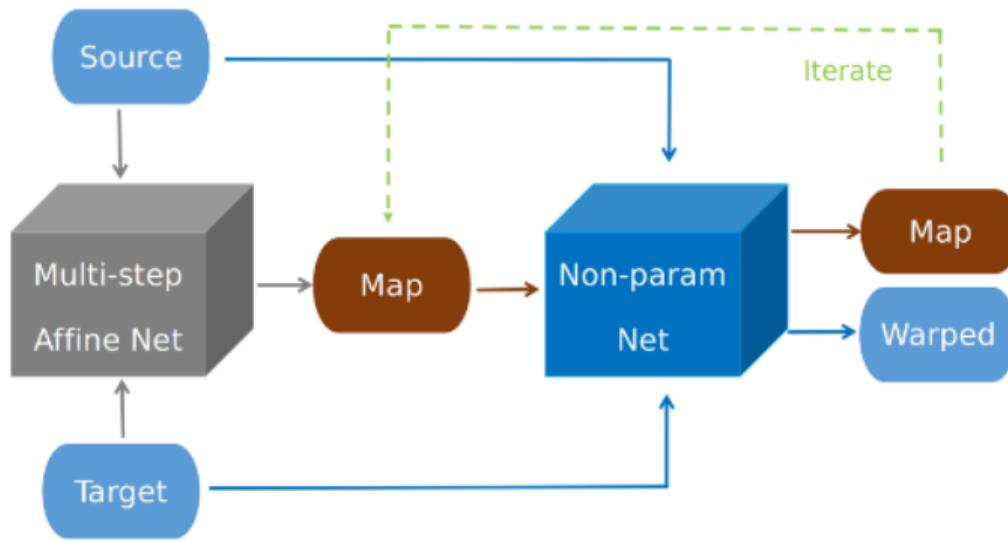
$$\begin{aligned} L_a(M, T, \Gamma, \Gamma^{tm}) = & L_{a-sim}(M, T, \Gamma) + L_{a-sim}(T, M, \Gamma^{tm}) + \\ & L_{a-reg}(\Gamma) + L_{a-reg}(\Gamma^{tm}) + \\ & L_{a-sym}(\Gamma, \Gamma^{tm}) \end{aligned}$$

ASVM - multi-step non-rigid registration



⁴Shen et al. 2019.

RDMM - Region-specific Diffeomorphic Metric Mapping



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⁵Zhengyang Shen, François-Xavier Vialard, and Marc Niethammer. 2019.
“Region-specific Diffeomorphic Metric Mapping.” *NeurIPS: Neural Information Processing Systems*.

$$v(x, t) = K(x, t) \star m = \sum_{i_0}^{N-1} w_i(x, t) K_{\sigma_i} \star (w_i(x, t)m), \quad w_i(x, t) \geq 1$$

$$v(x, t) = K(x, t) \star m = \sum_{i_0}^{N-1} w_i(x, t) K_{\sigma_i} \star (w_i(x, t)m), \quad w_i(x, t) \geq 1$$

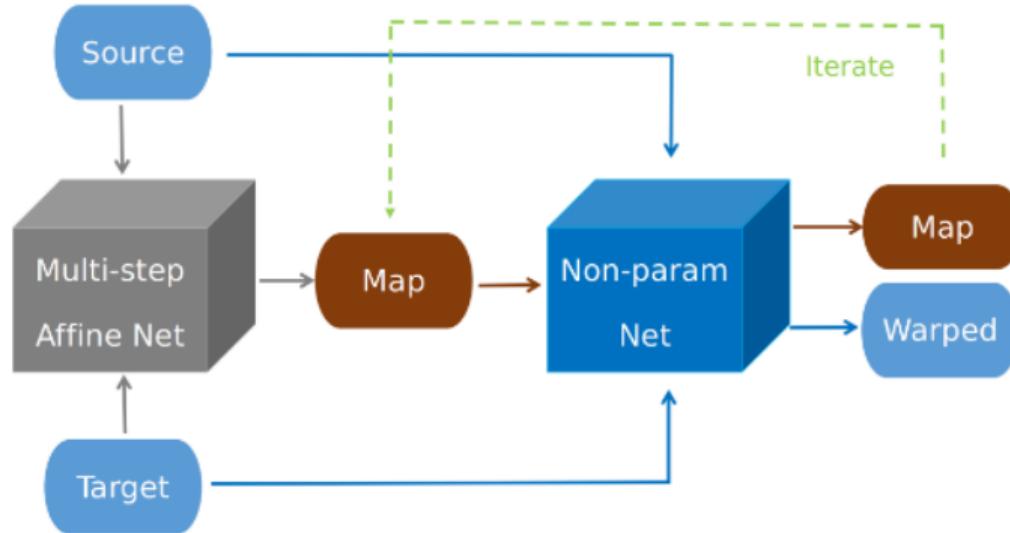
$$w_i(x, 0) = G_\sigma h_i(x, 0) \quad s.t. \quad h_i(x, 0) \geq 0$$

$$v(x, t) = K(x, t) \star m = \sum_{i_0}^{N-1} w_i(x, t) K_{\sigma_i} \star (w_i(x, t)m), \quad w_i(x, t) \geq 1$$

$$w_i(x, 0) = G_\sigma h_i(x, 0) \quad s.t. \quad h_i(x, 0) \geq 0$$

$$Reg(\{h_i(x, 0)\}, T) = \lambda_{OMT}(T) OMT(\{h_i(x, 0)\}) + \lambda_{Range}(T) Range(\{h_i(x, 0)\})$$

RDMM

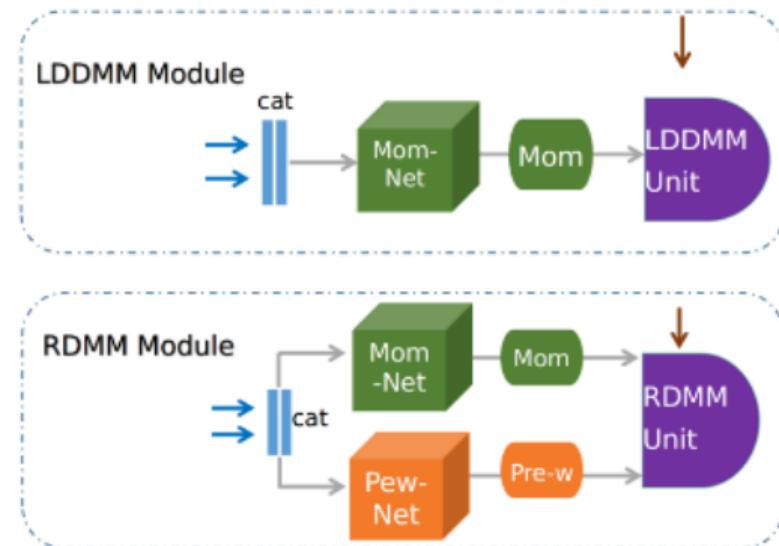
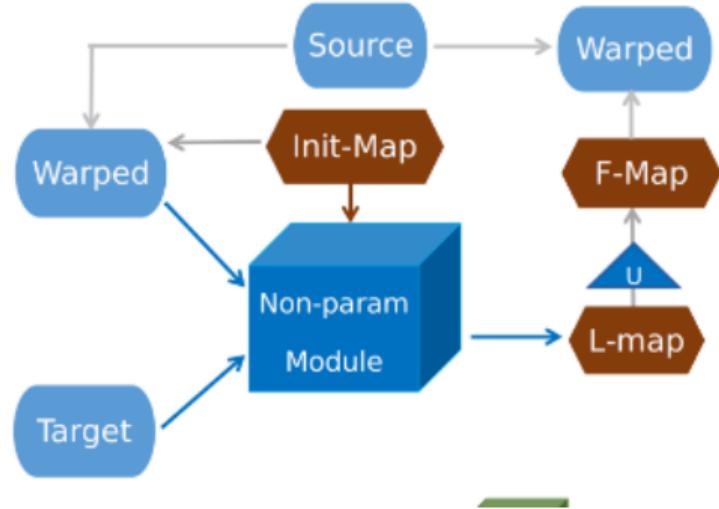


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⁶Shen, Vialard, and Niethammer 2019.

RDMM

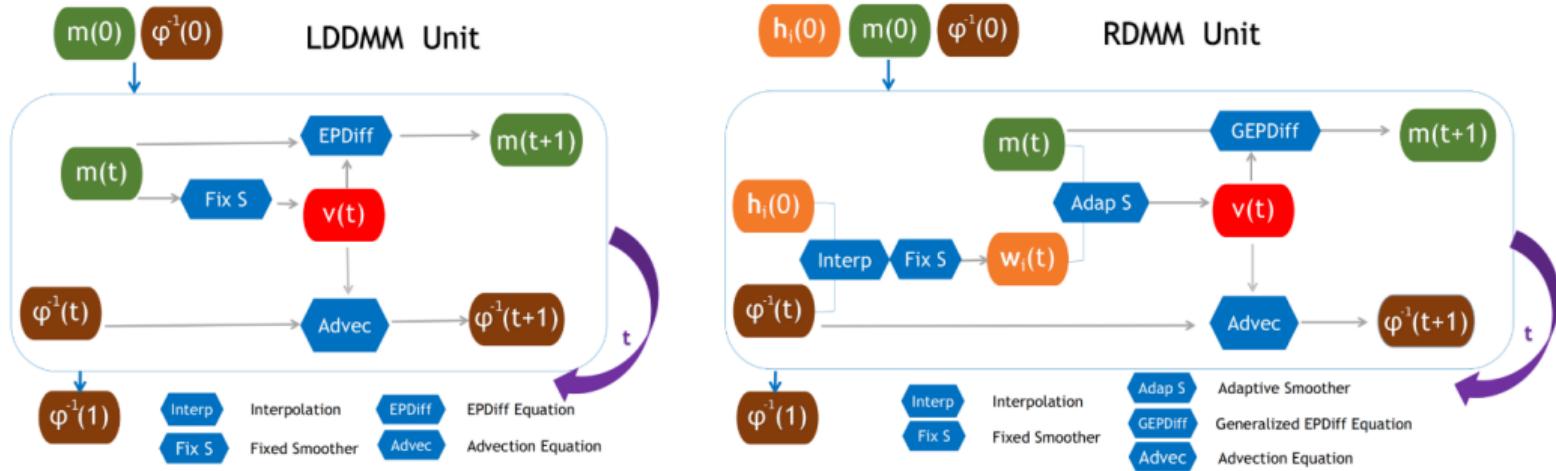
Non-parametric Network



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⁷Shen, Vialard, and Niethammer 2019.

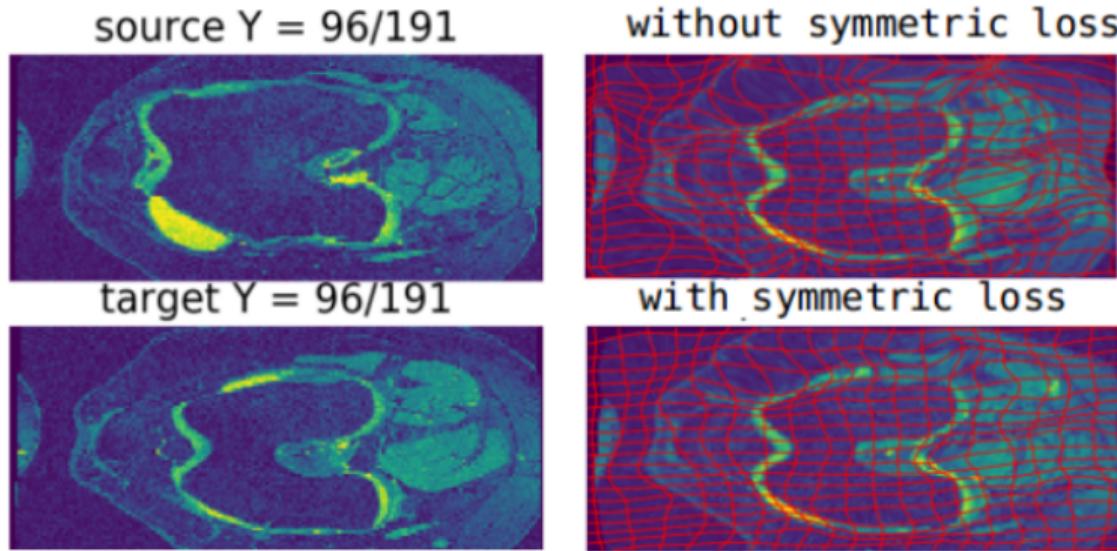
RDMM



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⁸Shen, Vialard, and Niethammer 2019.

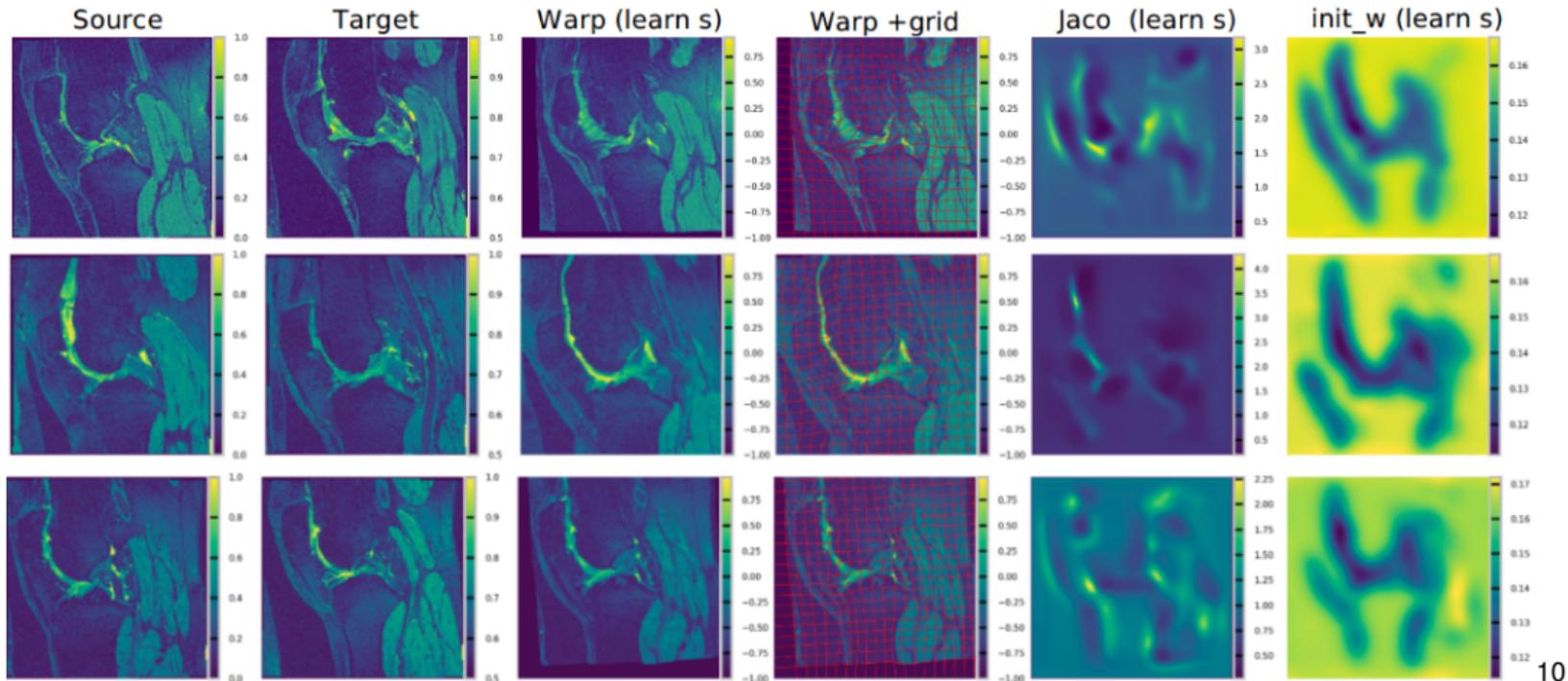
Results - ASVM



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⁹Shen et al. 2019.

Results - RDMM



¹⁰Shen, Vialard, and Niethammer 2019.

Results - RDMM

RDMM with pre-defined regularizer ↗

Outline

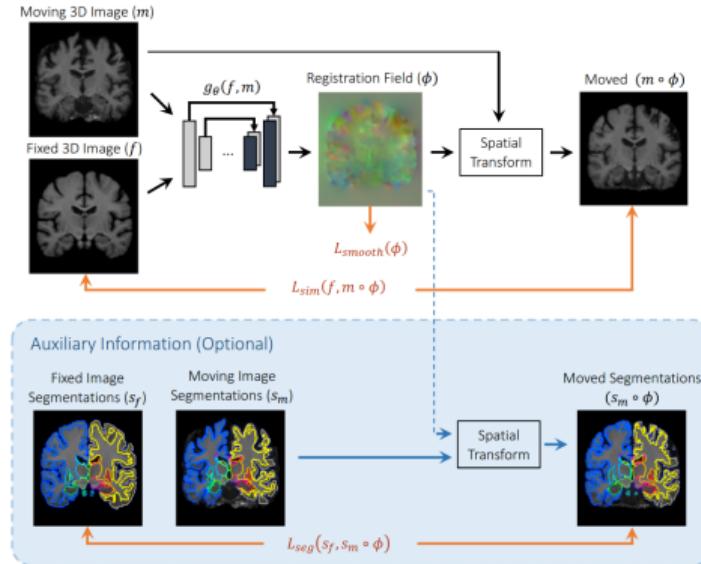
1. Mermaid

2. Voxelmorph

Voxelmorph

- unsupervised NN Voxelmorph
- Probabilistic version
- Learning conditional and unconditional templates
- Learning image registration with synthetic data SynthMorph
- Learning Hyperparameters HyperMorph

Voxelmorph base model

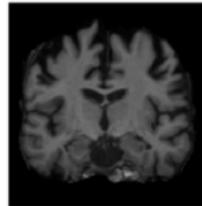


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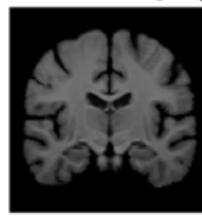
¹¹Guha Balakrishnan et al. 2019. “Voxelmorph: A Learning Framework for Deformable Medical Image Registration.” *IEEE TMI: Transactions on Medical Imaging* 38 (8): 1788–1800.

Probabilistic Voxelmorph

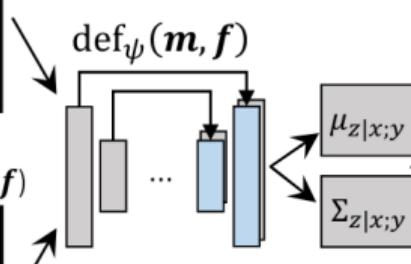
Moving 3D Image (\mathbf{m})



Fixed 3D Image (\mathbf{f})



$\text{def}_\psi(\mathbf{m}, \mathbf{f})$

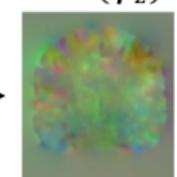


velocity field

Z

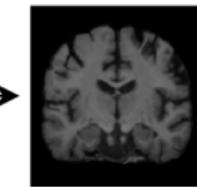
integration
layer

deformation
field (ϕ_z)



Spatial
Transform

Moved ($\mathbf{m} \circ \phi_z$)



Loss (\mathcal{L})

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¹²Adrian V. Dalca et al. 2019b. “Unsupervised Learning of Probabilistic Diffeomorphic Registration for Images and Surfaces.” *Medical Image Analysis* 57:226–236.

Probabilistic Voxelmorph

Goal:

$$p(z|T, M)$$

Probabilistic Voxelmorph

Goal:

$$p(z|T, M)$$

prior:

$$p(z) = \mathcal{N}(z, 0; \Sigma_z)$$

Probabilistic Voxelmorph

Goal:

$$p(z|T, M)$$

prior:

$$p(z) = \mathcal{N}(z, 0; \Sigma_z)$$

approximation:

$$q_\psi(z | T; M) = \mathcal{N}(z; \mu_{z|T,M}, \Sigma_{z|T,M})$$

Probabilistic Voxelmorph

Goal:

$$p(z|T, M)$$

prior:

$$p(z) = \mathcal{N}(z, 0; \Sigma_z)$$

approximation:

$$q_\psi(z | T; M) = \mathcal{N}(z; \mu_{z|T,M}, \Sigma_{z|T,M})$$

negative variational lower bound:

$$\min_\psi KL [q_\psi(z | T; M) \| p(z)] - \mathbb{E}_q [\log p(T | z, M)]$$

Probabilistic Voxelmorph

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$$p(z|T, M)$$

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$$q_\psi(z | T; M) = \mathcal{N}(z; \mu_{z|T,M}, \Sigma_{z|T,M})$$

negative variational lower bound:

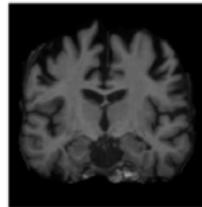
$$\min_\psi KL [q_\psi(z | T; M) \| p(z)] - \mathbb{E}_q [\log p(T | z, M)]$$

target image:

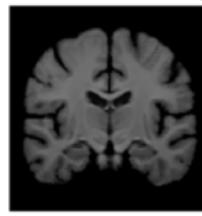
$$p(T | z; M) = \mathcal{N}(T; M \circ \varphi, \sigma_I^2 \mathcal{I})$$

Probabilistic Voxelmorph

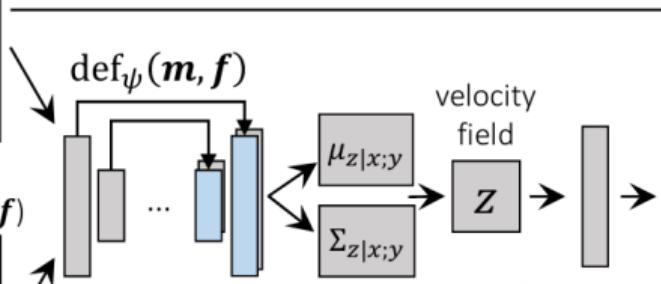
Moving 3D Image (\mathbf{m})



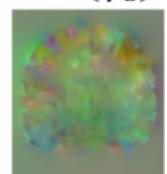
Fixed 3D Image (\mathbf{f})



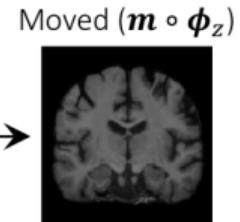
$\text{def}_{\psi}(\mathbf{m}, \mathbf{f})$



deformation
field (ϕ_z)



Spatial
Transform



Loss (\mathcal{L})

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¹³Adrian V. Dalca et al. 2019b.

Probabilistic Voxelmorph + segmentation

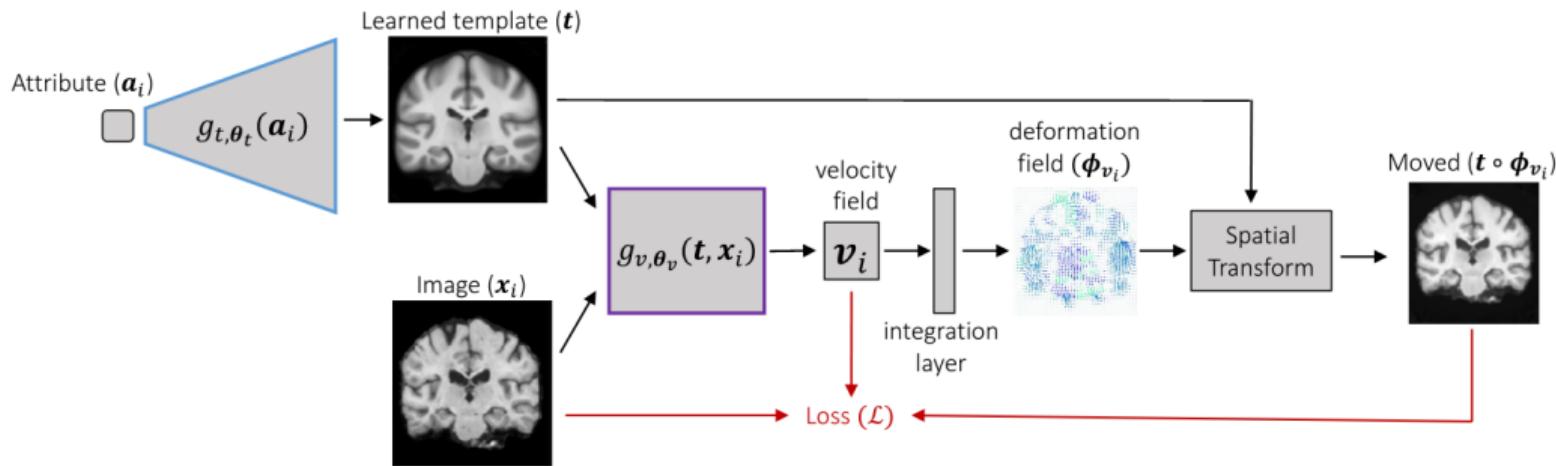
extend negative lower bound:

$$NLB - \mathbb{E}_q [\log p(s_T \mid z; s_M)]$$

segmentation target image:

$$p(s_T \mid z; s_M) = \mathcal{N}(s_T; s_M \circ \varphi_z, \sigma_s^2 \mathcal{I})$$

Conditional and unconditional atlases



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¹⁴Adrian V Dalca et al. 2019a. “Learning Conditional Deformable Templates with Convolutional Networks.” *NeurIPS: Neural Information Processing Systems*.

Conditional and unconditional atlases

$$\begin{aligned} L(\theta_t, \theta_v, v_i, x_i, a_i) &= -\log p_\theta(x_i \mid v_i, a_i) - \log p_\theta(v_i) \\ &= -\frac{1}{2\sigma^2} \|x_i - g_{t,\theta_t}(a_i) \circ \varphi_{v_i}\|^2 \\ &\quad - \gamma \|\bar{u}\|^2 - \lambda_d \frac{d}{2} \sum_i \|u_i\|^2 + \frac{\lambda_a}{2} \sum_i \|\nabla u_i\|^2 \end{aligned}$$

Conditional and unconditional atlases

$$p_{\theta}(V) \propto \exp\{-\gamma \|\bar{u}\|^2\} \prod_i \mathcal{N}(u_i, 0, \Sigma_u)$$

$$\bar{u} = \frac{1}{n} \sum_i u_i$$

$$\Sigma_u^{-1} = \lambda_d D - \lambda_a C$$

Conditional and unconditional atlases

$$p_{\theta}(V) \propto \exp\{-\gamma \|\bar{u}\|^2\} \prod_i \mathcal{N}(u_i, 0, \Sigma_u)$$

$$\bar{u} = \frac{1}{n} \sum_i u_i$$

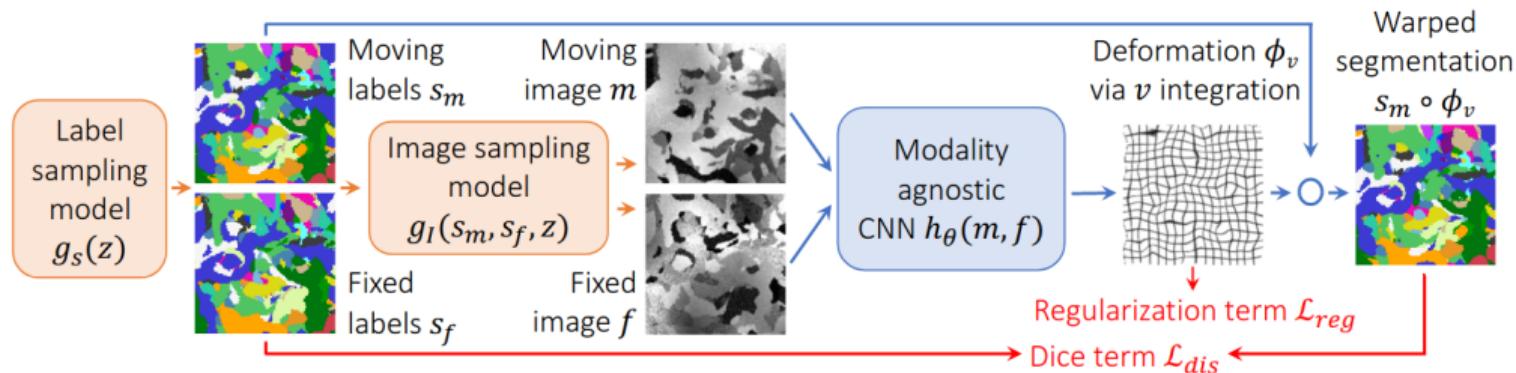
$$\Sigma_u^{-1} = \lambda_d D - \lambda_a C$$

$$\log p_{\theta}(V) = -\gamma \|\bar{u}\|^2 - \lambda_d \frac{d}{2} \sum_i \|u_i\|^2 + \frac{\lambda_a}{2} \sum_i \|\nabla u_i\|^2$$

Conditional and unconditional atlases

$$\begin{aligned} L(\theta_t, \theta_v, v_i, x_i, a_i) &= -\log p_\theta(x_i \mid v_i, a_i) - \log p_\theta(v_i) \\ &= -\frac{1}{2\sigma^2} \|x_i - g_{t,\theta_t}(a_i) \circ \varphi_{v_i}\|^2 \\ &\quad - \gamma \|\bar{u}\|^2 - \lambda_d \frac{d}{2} \sum_i \|u_i\|^2 + \frac{\lambda_a}{2} \sum_i \|\nabla u_i\|^2 \end{aligned}$$

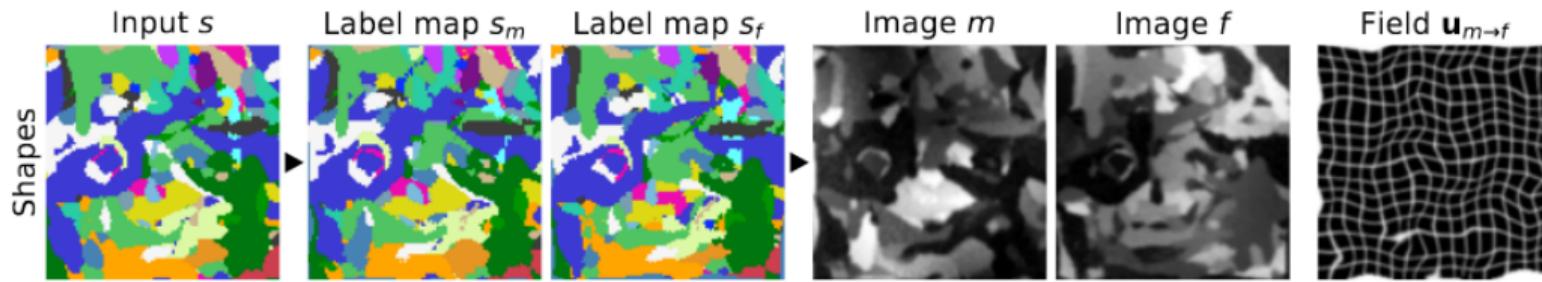
SynthMorph



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¹⁵Malte Hoffmann et al. 2020. *Learning image registration without images*. arXiv: 2004.10282 [cs.CV] ↗.

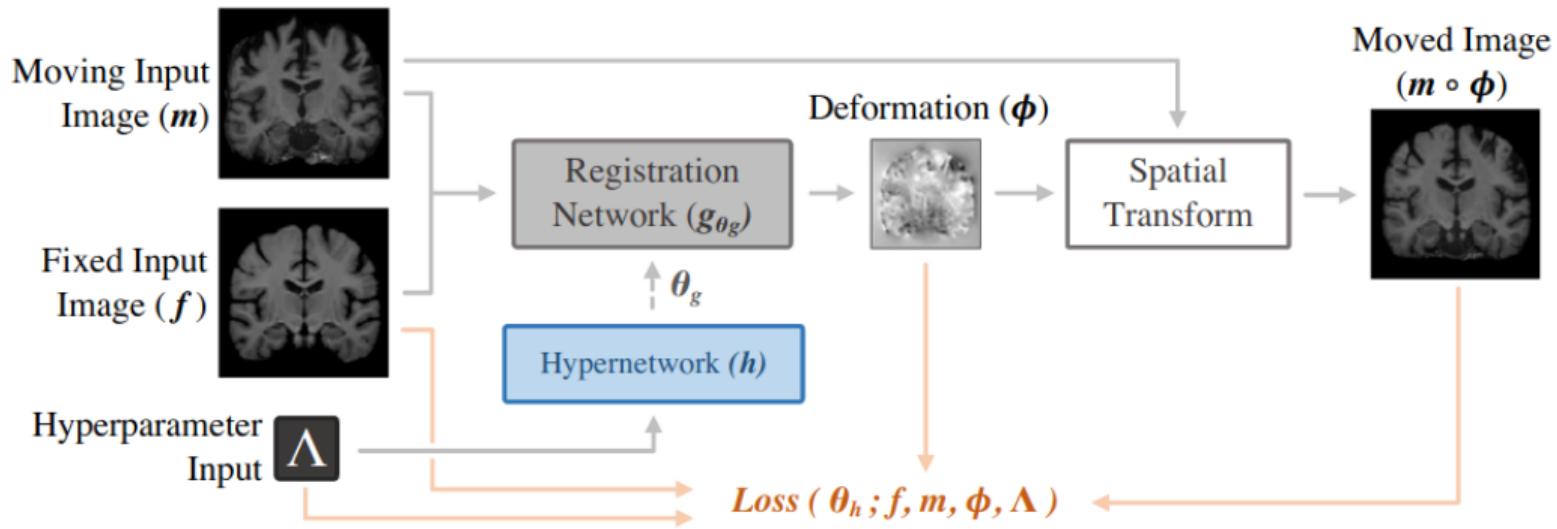
SynthMorph



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¹⁶Hoffmann et al. 2020.

Hypermorph



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¹⁷ Andrew Hoopes et al. 2021. "HyperMorph: Amortized Hyperparameter Learning for Image Registration." *arXiv preprint arXiv:2101.01035*.

HyperMorph

$$L_h(\theta_h; D) = \mathbb{E}_{\Lambda \sim p(Lambda)} [L(\theta_h; D, \Lambda)]$$

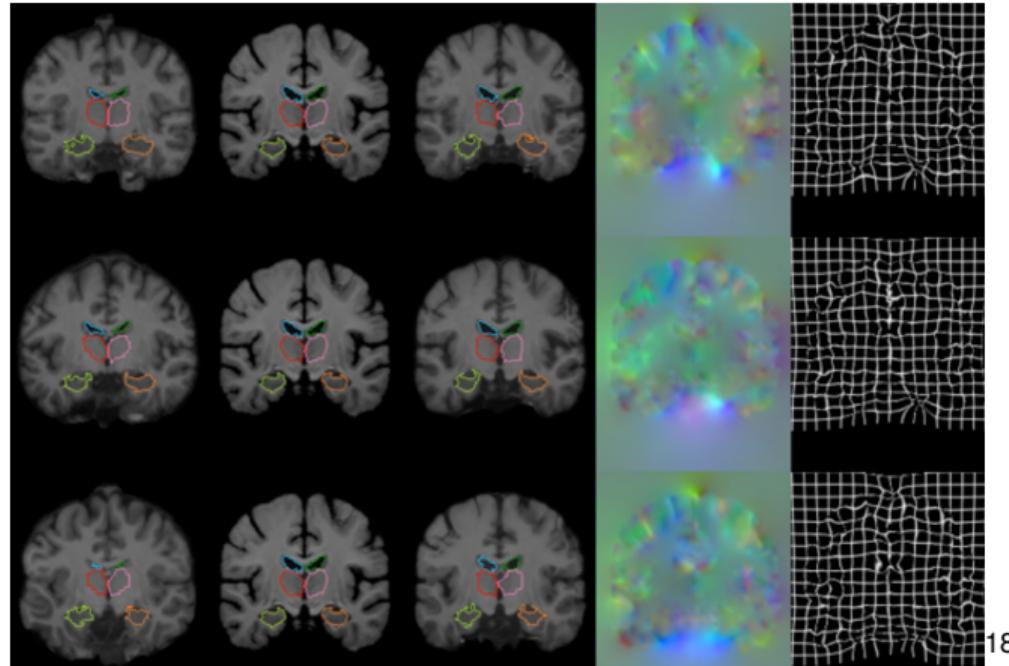
HyperMorph

$$L_h(\theta_h; D) = \mathbb{E}_{\Lambda} \left[\sum_{M, T \in D} ((1 - \lambda) L_{sim}(T, M \circ \varphi; \lambda_{sim}) + \lambda L_{reg}(\varphi; \lambda_{reg})) \right]$$

HyperMorph

$$\begin{aligned} L_h(\theta_h; D) = \mathbb{E}_{\Lambda} \sum_{M, T \in D} & [(1 - \lambda)(1 - \gamma)L_{sim}(T, M \circ \varphi; \lambda_{sim})] \\ & + \lambda L_{reg}(\varphi; \lambda_{reg}) + (1 - \lambda)\gamma L_{seg}(s_T, s_M \circ \varphi)] \end{aligned}$$

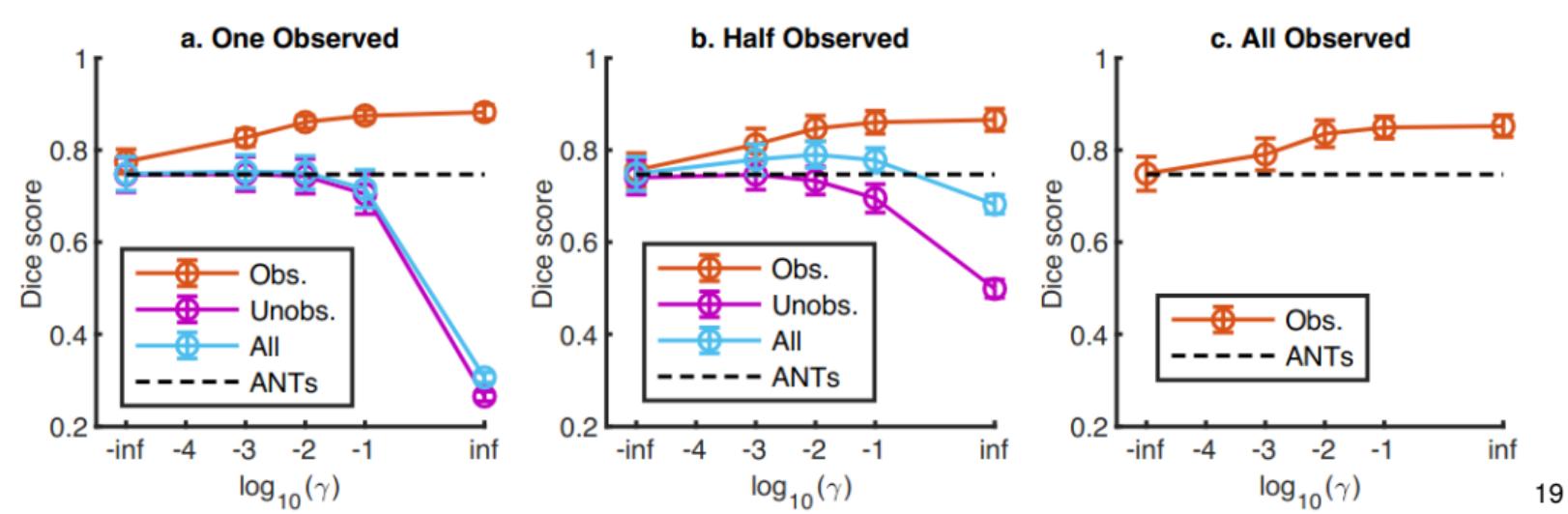
Results - Voxelmorph



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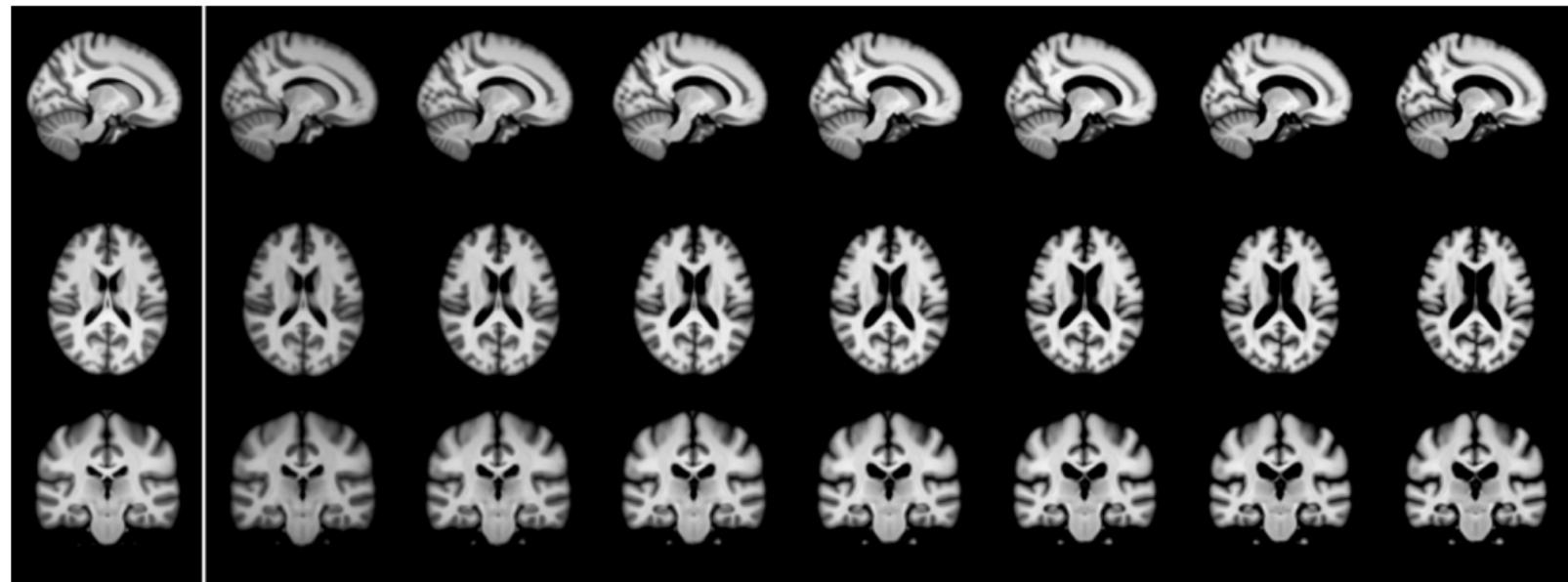
¹⁸Balakrishnan et al. 2019.

Results - Voxelmorph



¹⁹Balakrishnan et al. 2019.

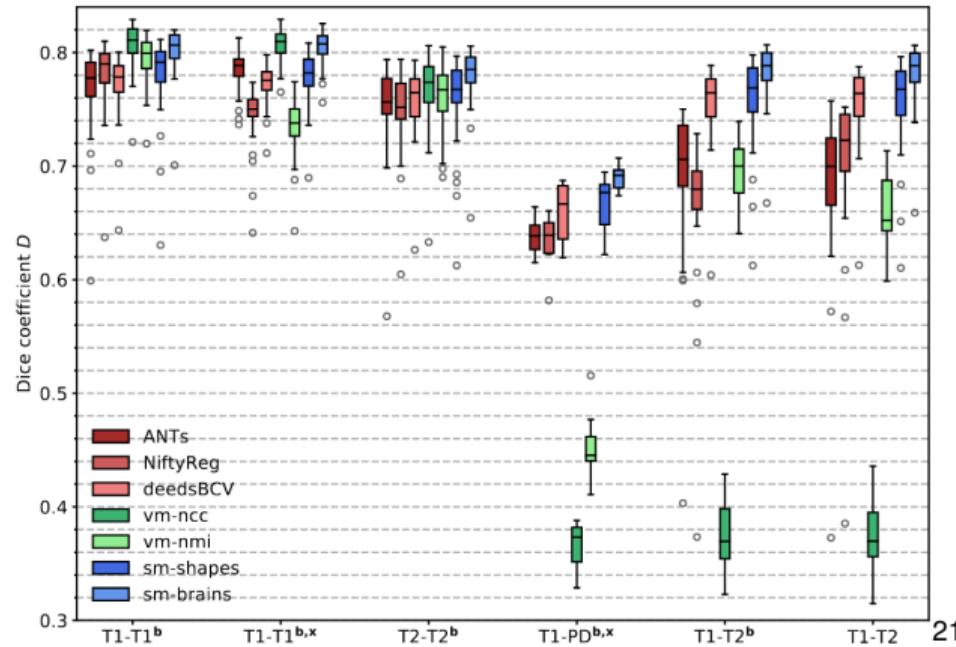
Results - Atlases



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²⁰Adrian V Dalca et al. 2019a.

Results - Synthmorph



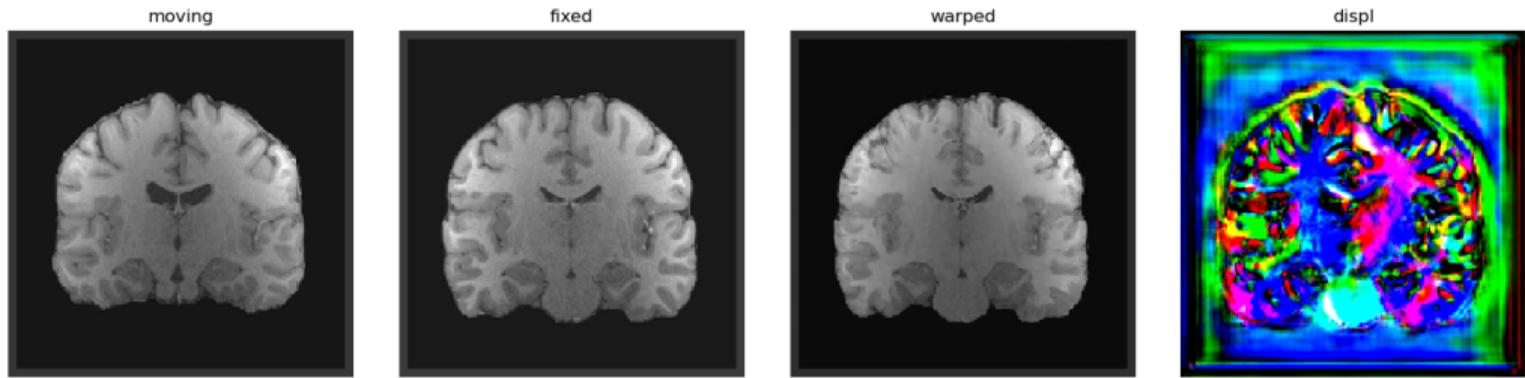
²¹Hoffmann et al. 2020.

Experiments

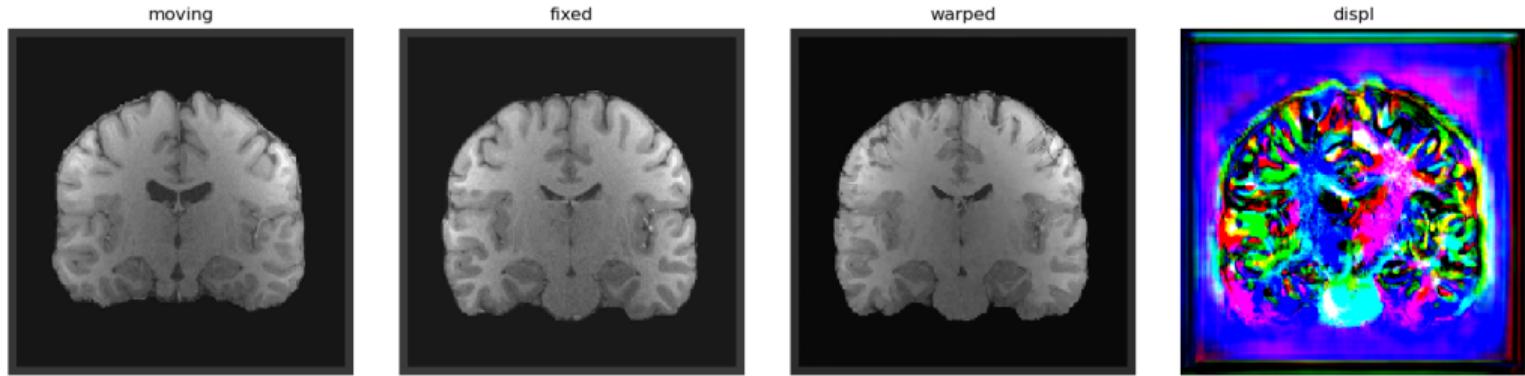
Preprocessing

1. skull-stripping
2. affine alignment
3. intensity normalization

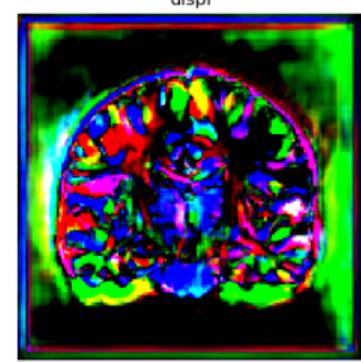
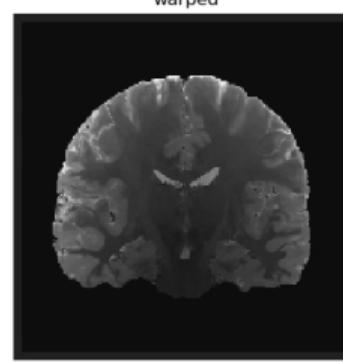
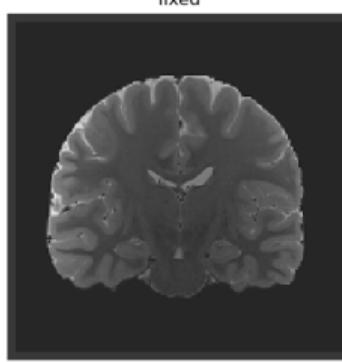
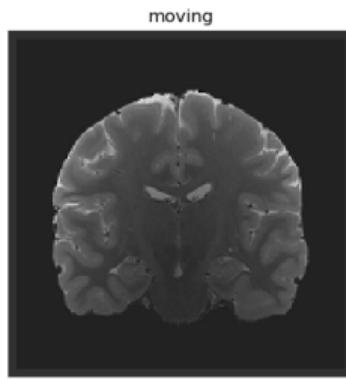
intra-modal T1w brain scans 40 epochs



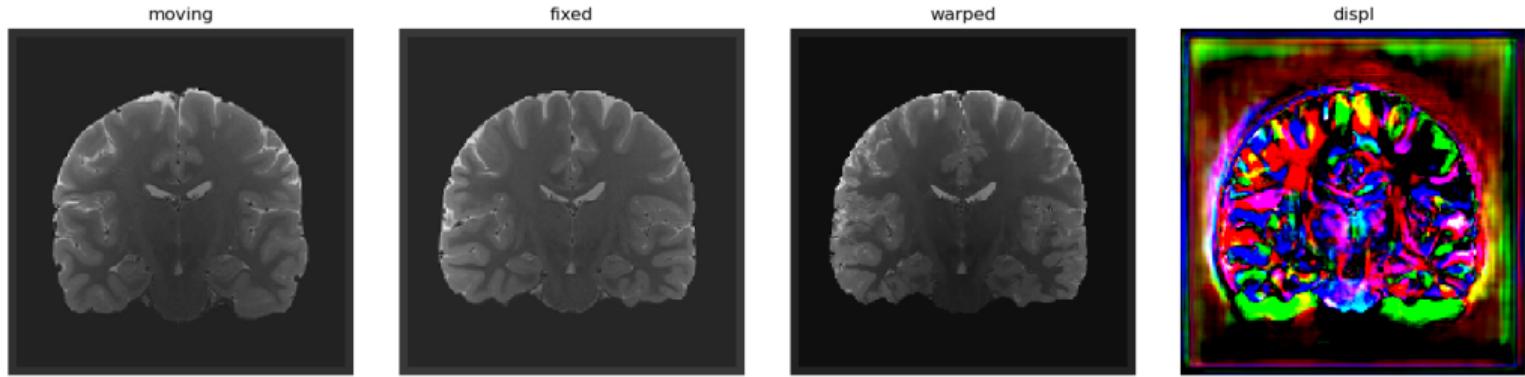
intra-modal T1w brain scans 80 epochs



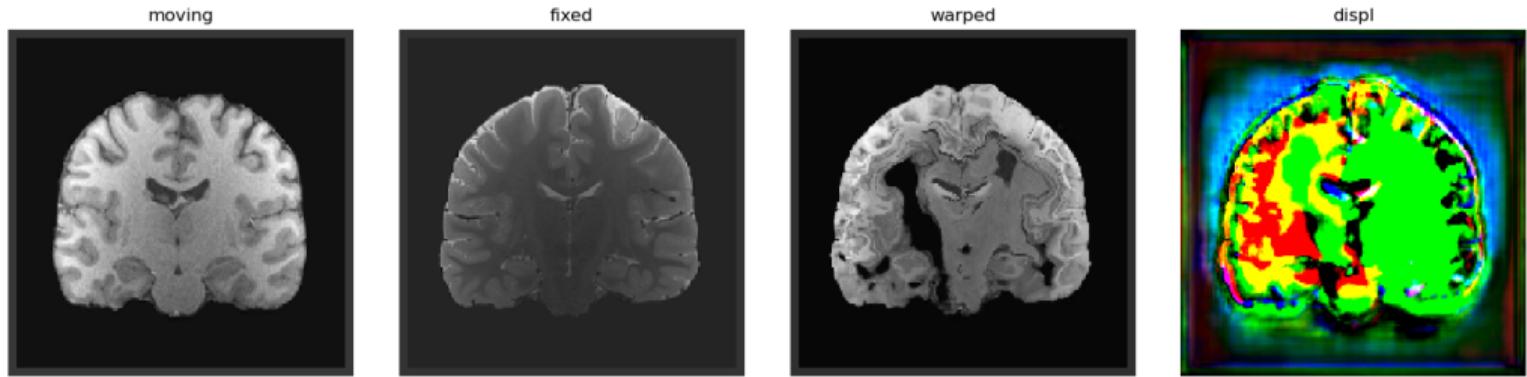
intra-modal T2w brain scans 40 epochs



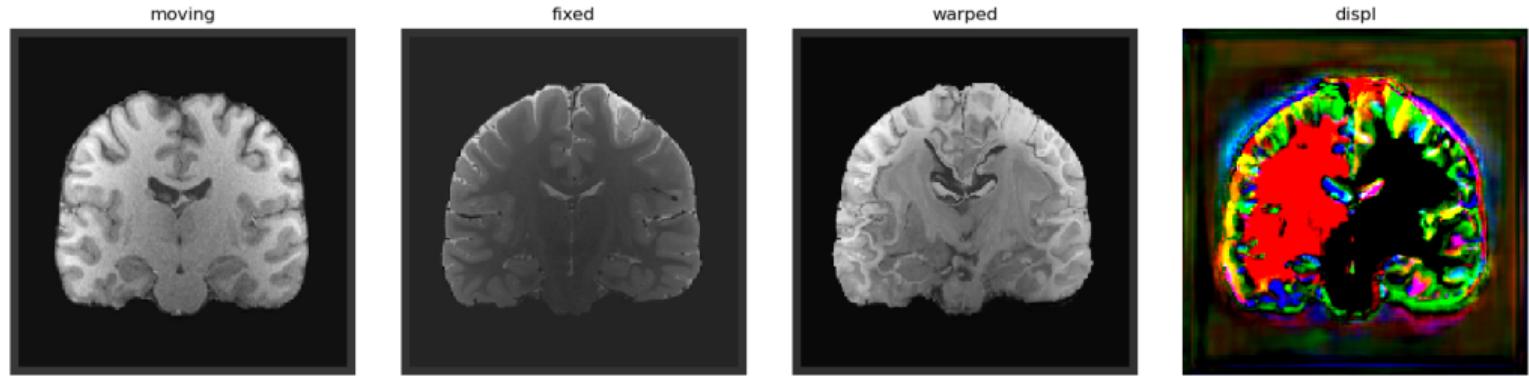
intra-modal T2w brain scans 80 epochs



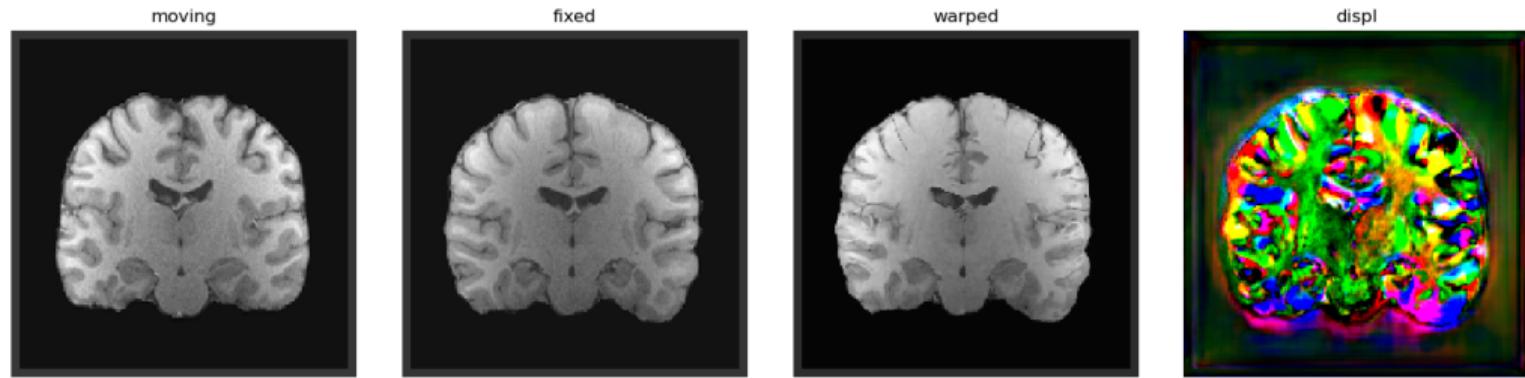
inter-modal T1w-T2w brain scans 40 epochs



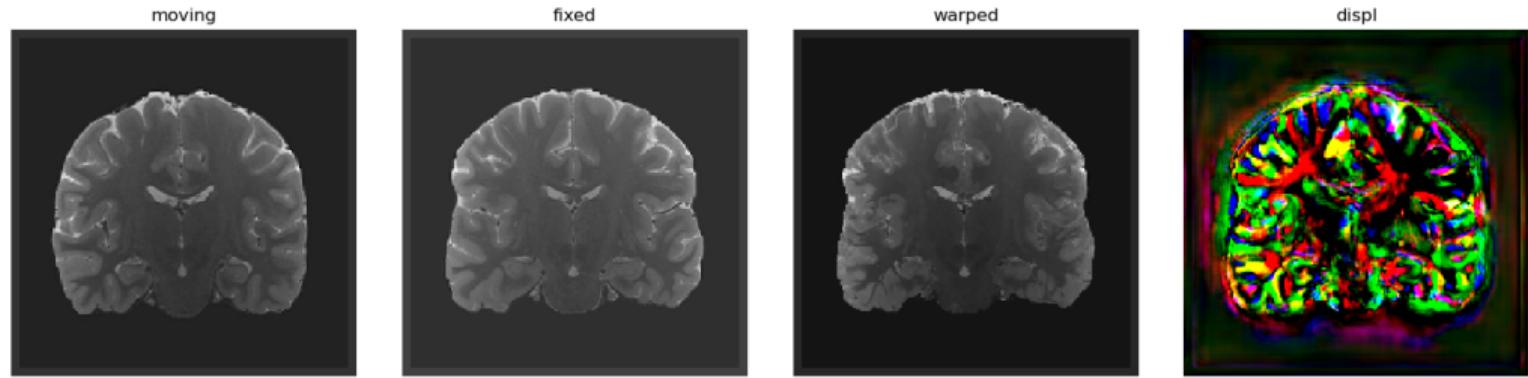
inter-modal T1w-T2w brain scans 80 epochs



intra-modal T1w-T1w brain scans 80 epochs



intra-modal T2w-T2w brain scans 80 epochs



References I

-  Balakrishnan, Guha, Amy Zhao, Mert Sabuncu, John Guttag, and Adrian V. Dalca. 2018. “An Unsupervised Learning Model for Deformable Medical Image Registration.” *CVPR: Computer Vision and Pattern Recognition*, 9252–9260.
-  Balakrishnan, Guha, Amy Zhao, Mert Sabuncu, John Guttag, and Adrian V. Dalca. 2019. “VoxelMorph: A Learning Framework for Deformable Medical Image Registration.” *IEEE TMI: Transactions on Medical Imaging* 38 (8): 1788–1800.
-  Dalca, Adrian V, Marianne Rakic, John Guttag, and Mert R Sabuncu. 2019a. “Learning Conditional Deformable Templates with Convolutional Networks.” *NeurIPS: Neural Information Processing Systems*.

References II

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- Dalca, Adrian V., Guha Balakrishnan, John Guttag, and Mert R Sabuncu. 2018. “Unsupervised Learning for Fast Probabilistic Diffeomorphic Registration.” *MICCAI: Medical Image Computing and Computer Assisted Intervention, LNCS* 11070:729–738.
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- Isensee, Fabian, Marianne Schell, Irada Pflueger, Gianluca Brugnara, David Bonekamp, Ulf Neuberger, Antje Wick, et al. 2019. *Automated brain extraction of multi-sequence MRI using artificial neural networks*, August.
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-  Shen, Zhengyang, Xu Han, Zhenlin Xu, and Marc Niethammer. 2019. "Networks for Joint Affine and Non-parametric Image Registration." In *Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition*, 4224–4233.
-  Shen, Zhengyang, François-Xavier Vialard, and Marc Niethammer. 2019. "Region-specific Diffeomorphic Metric Mapping." *NeurIPS: Neural Information Processing Systems*.

References V

- Yang, Xiao, Roland Kwitt, and Marc Niethammer. 2016. “Fast Predictive Image Registration.” In *DLMIA: International Workshop on Deep Learning in Medical Image Analysis*, 48–57.
- Yang, Xiao, Roland Kwitt, Martin Styner, and Marc Niethammer. 2017. “Quicksilver: Fast predictive image registration—a deep learning approach.” *NeuroImage* 158:378–396.

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