



Deep Bilevel Optimization Learning for Medical Image Registration

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Outline

- ① **Background**
- ② **Bilevel Feature Learning for Image Registration**
- ③ **Optimization Learning for Deformable Image Registration**
- ④ **Automated Learning for Medical Image Registration**
- ⑤ **Summary and Outlook**

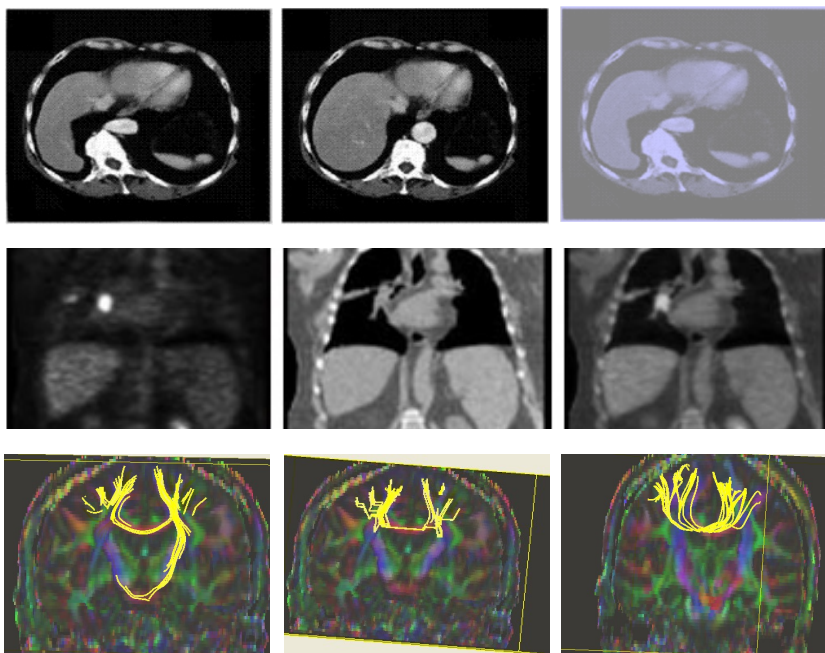


Background

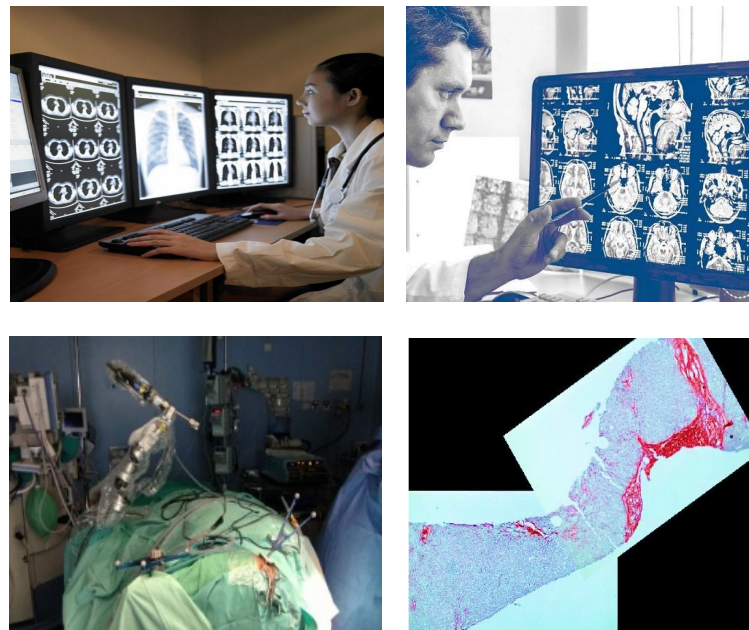
Medical Image Registration (MIR)

Background

Image Registration



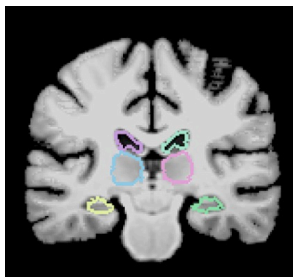
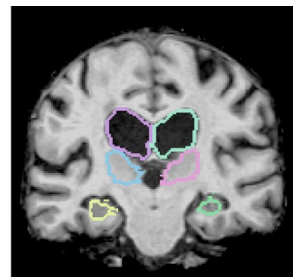
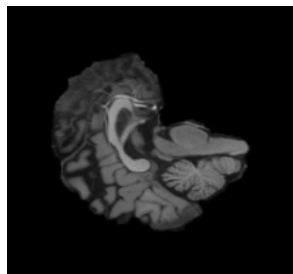
Diagnosis and Surgery



Problem Formulation

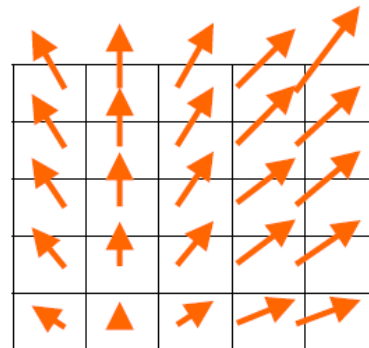
Objective of deformable registration

$$\min_{\varphi} \underbrace{E_D(\varphi; F, M(\varphi))}_{\text{Data Match}} + \lambda \underbrace{E_R(\varphi)}_{\text{Regularization}}$$

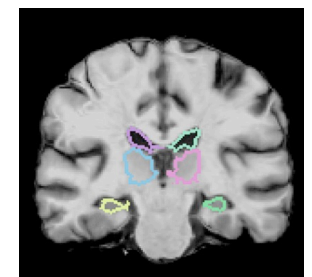
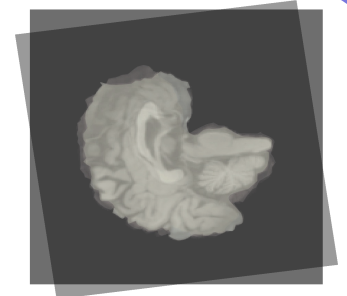


Moving

Fixed



Transformation Field



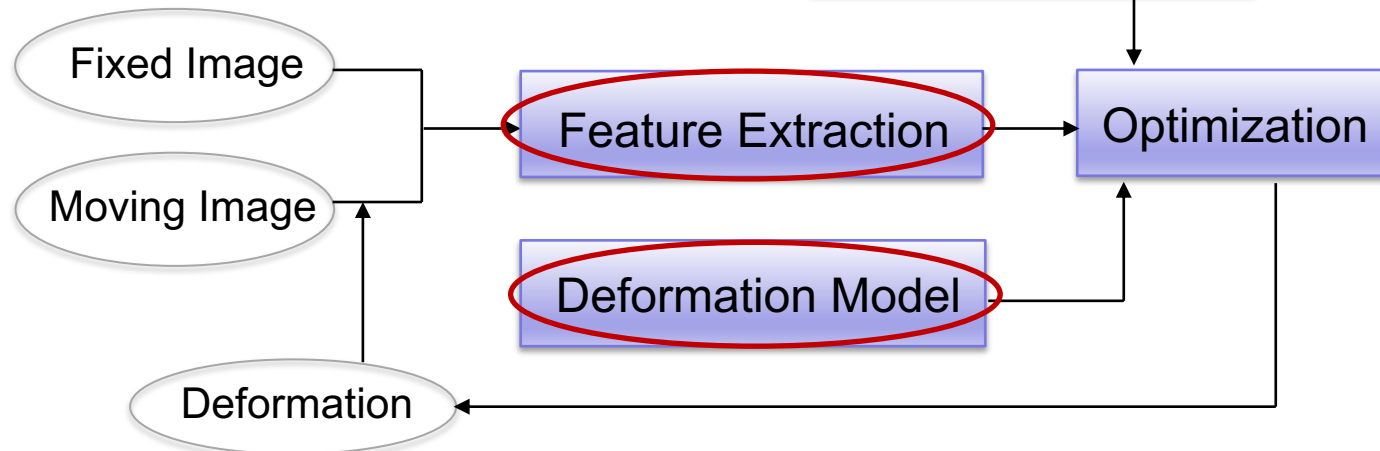
Warped

Problem Formulation

■ Objective of deformable registration

$$\min_{\varphi} \underbrace{E_D(\varphi; F, M(\varphi))}_{\text{Data Match}} + \lambda \underbrace{E_R(\varphi)}_{\text{Regularization}}$$

We need to construct three key components !

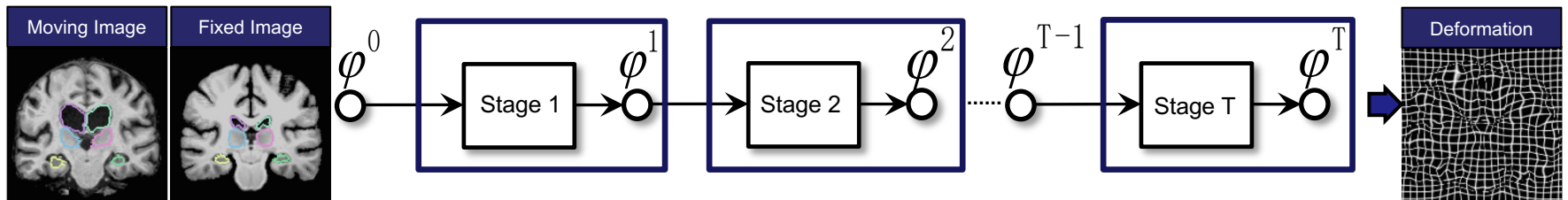


Related Works

■ Optimization based methods

Translate  into
knowledge

$$\min_{\varphi} \underbrace{E_D(\varphi; F, M(\varphi))}_{\text{Data Match}} + \lambda \underbrace{E_R(\varphi)}_{\text{Regularization}}$$



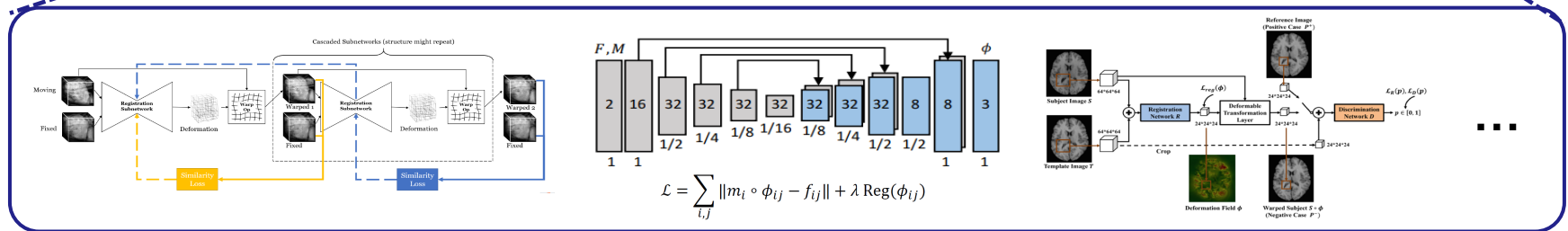
Satisfying accuracy



High computational cost

Related Works

Deep learning based methods



Fast estimate transformation



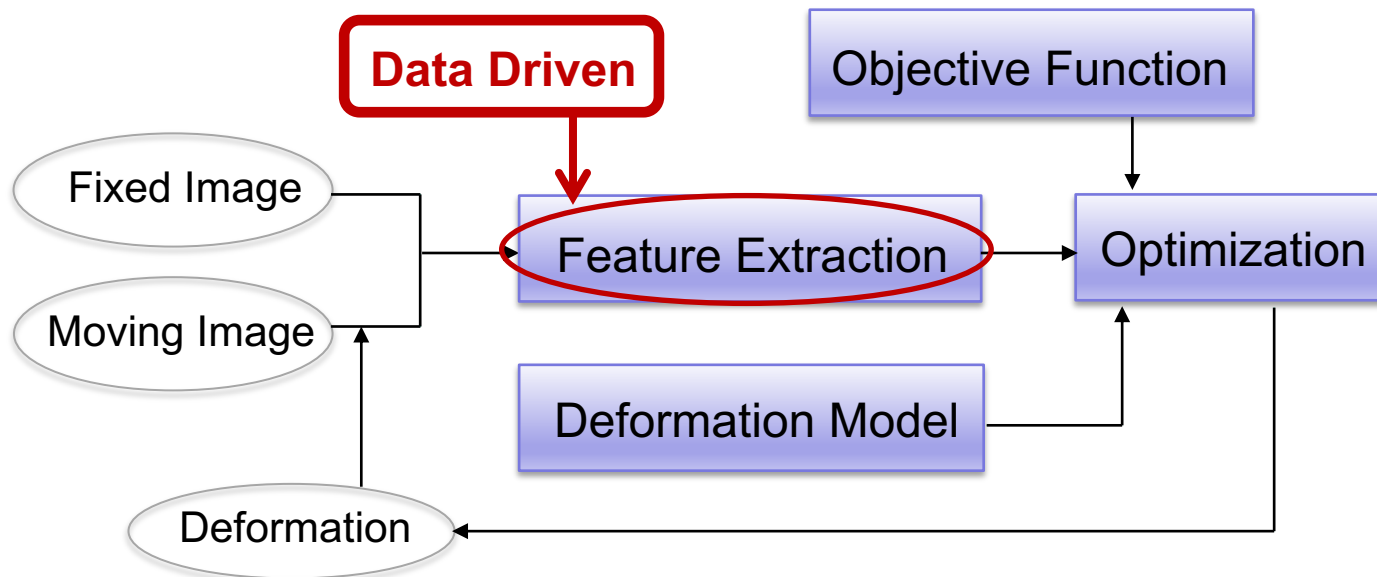
Ignore explicit constraints



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Motivation



Feature Learning for MIR

- **Upper-level:** Optimization of Deformable Registration
Lower-level: Probabilistic Feature Learning (**constraint**)

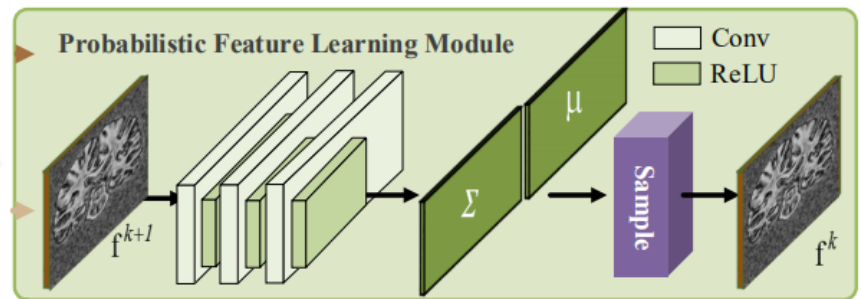
$$\min_{\varphi} E_D(\varphi; f_s, f_t) + E_R(\varphi),$$

$$s. t. f_s, f_t = \arg \max_{f_s, f_t} p(f_s | I_s, f_t | I_t, \varphi).$$

- **Probabilistic Feature Learning Module**

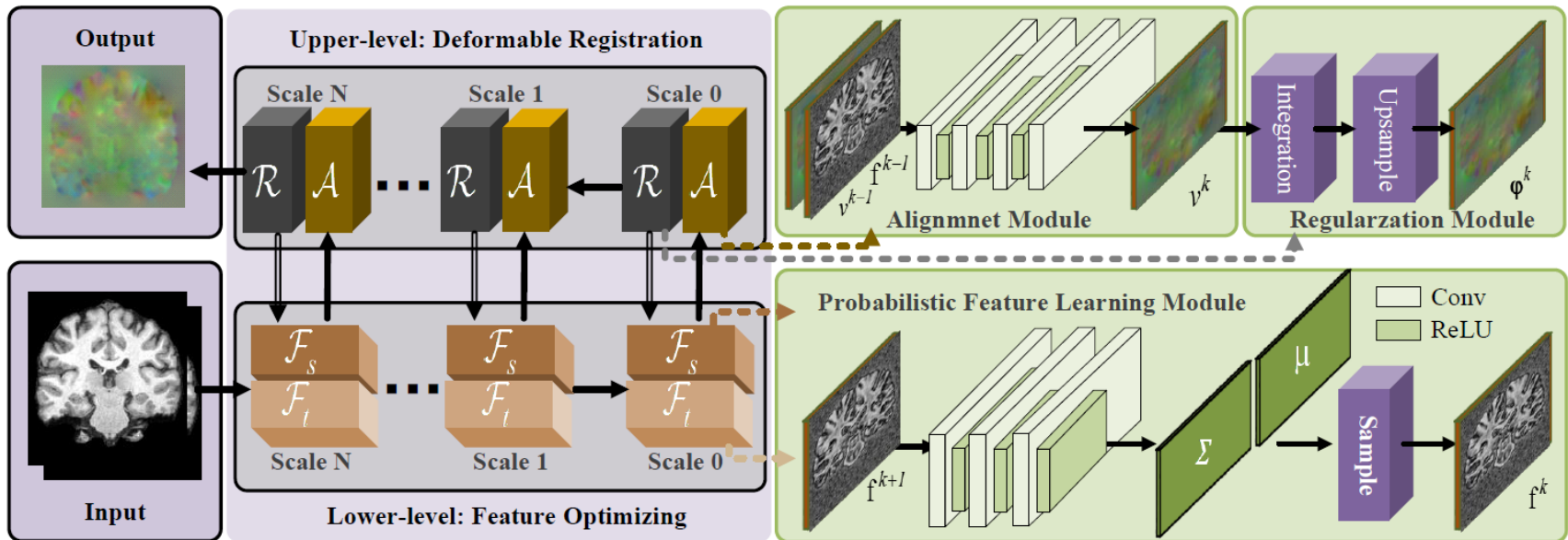
$$f = \arg \min_f \ln p(f | I, \varphi)$$

$$= \arg \min_f \underbrace{\ln p(I | f, \varphi)}_{\text{Data Likelihood}} + \underbrace{\ln p(f)}_{\text{Prior}}$$



Feature Learning for MIR

● Our Paradigm



Loss Function

Feature space: $l_{KL}(\mu, \Sigma) = 1/2(\text{tr}(\Sigma) + \|\mu\| - \log \det(\Sigma) - m)$

Image space: $l(I_s, I_t; \varphi) = l_{NCC}(I_s \circ \varphi, I_t) + l_{\text{smooth}}(\varphi).$

Feature Learning for MIR

◆ Quantitative comparison

Dice score	Elastix ^[1]	NiftyReg ^[2]	ANTs ^[3]	VM ^[4]	VM-diff ^[5]	Ours
OASIS	0.709	0.748	0.765	0.765	0.757	0.777
ABIDE	0.699	0.747	0.728	0.754	0.773	0.764
ADNI	0.697	0.737	0.761	0.761	0.768	0.773
PPMI	0.730	0.765	0.778	0.775	0.781	0.787

Runtime (s)	Elastix	NiftyReg	ANTs	VM	VM-diff	Ours
Img-to-Atlas	90	486	4529	0.615	0.512	0.351

[1] Elastix: A toolbox for intensity-based medical image registration.

[2] Free-form deformation using lower-order B-spline for nonrigid image registration.

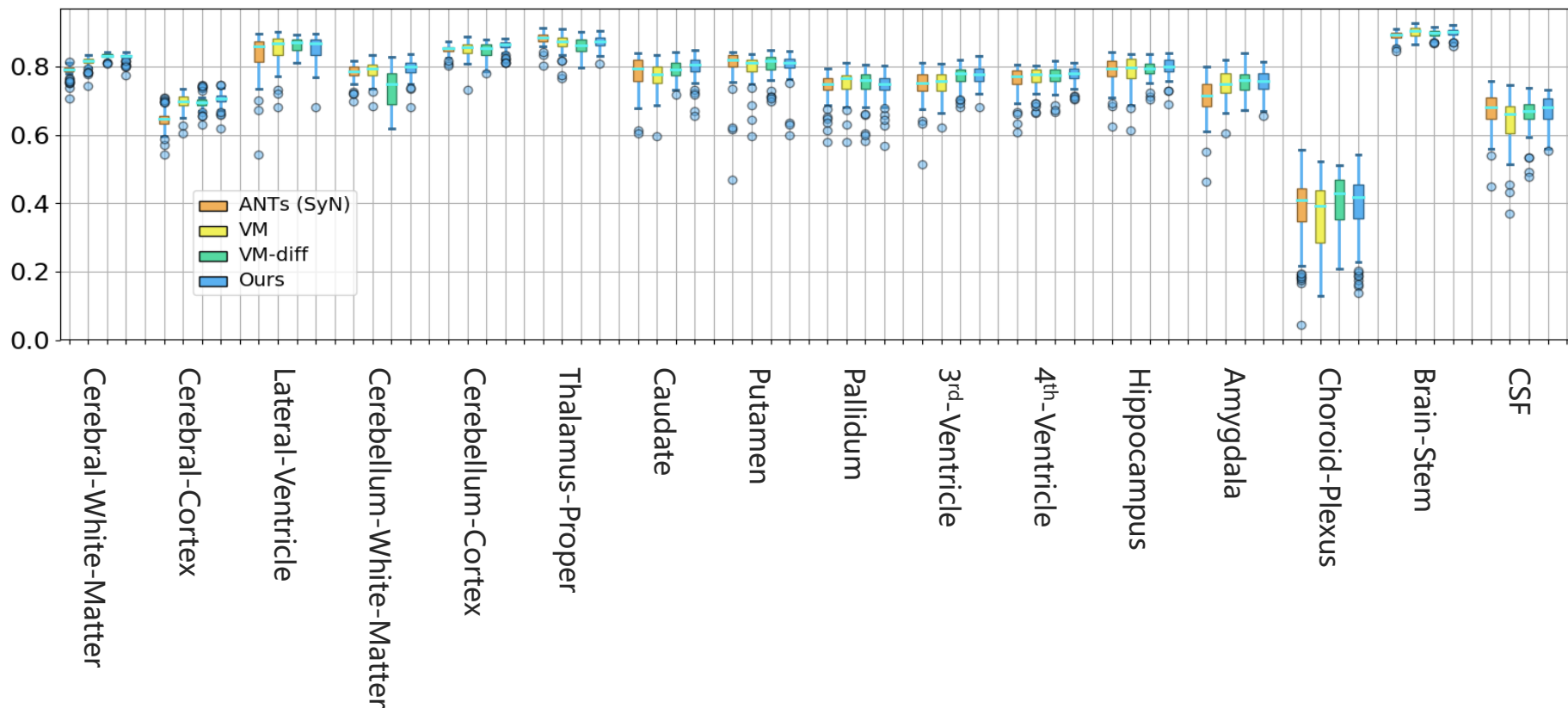
[3] A reproducible evaluation of ants similarity metric performance in brain image registration.

[4] Voxelmorph: A learning framework for deformable medical image registration.

[5] Unsupervised learning of probabilistic diffeomorphic registration for images and surfaces.

Feature Learning for MIR

◆ Visualizations of Dice score

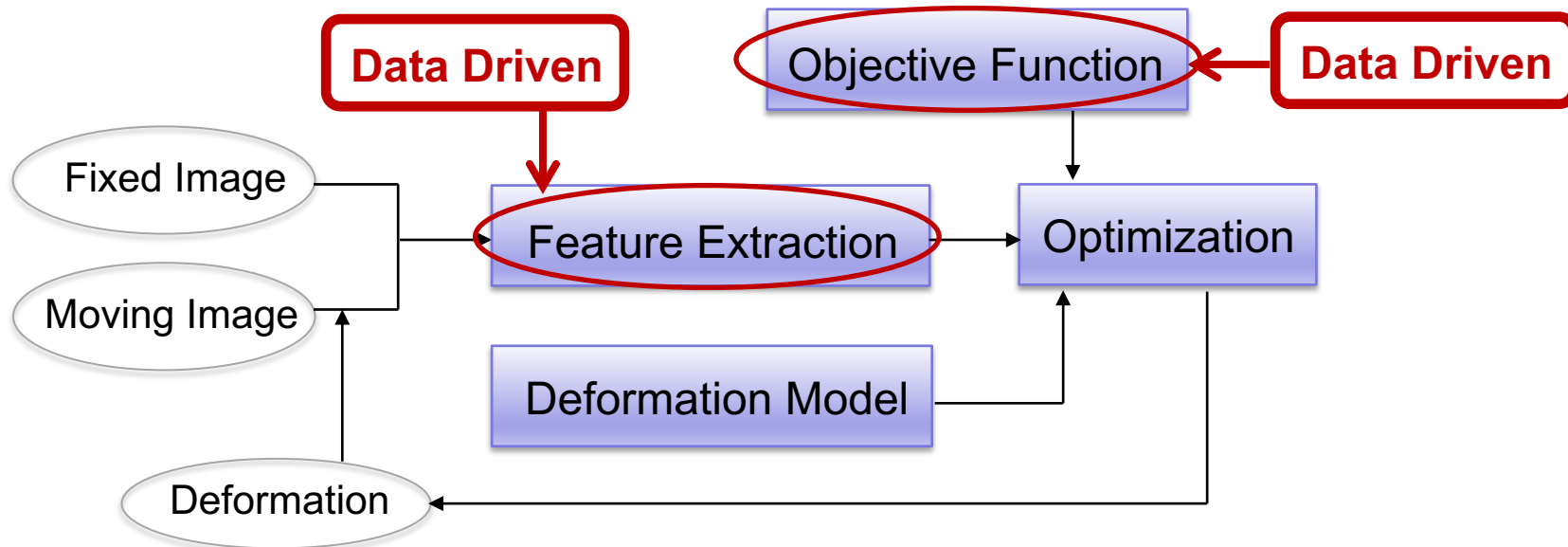




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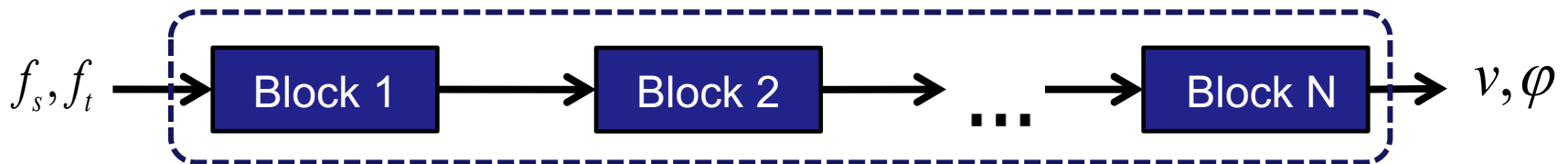


Optimization Learning for MIR

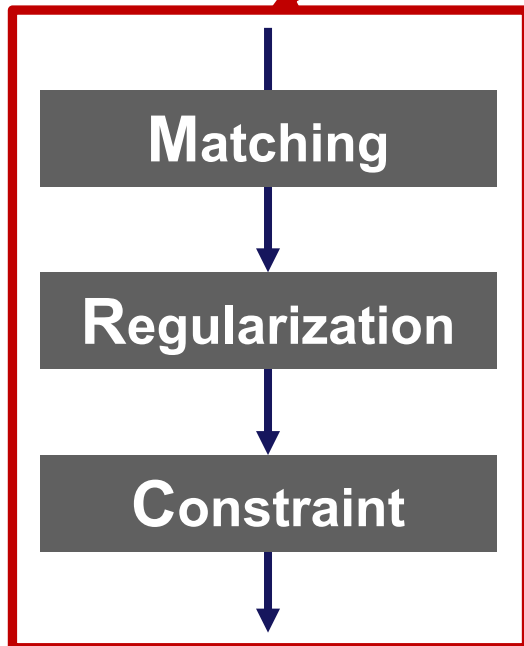
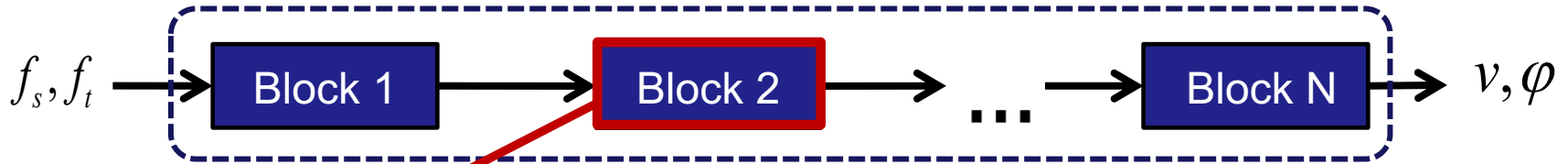
- **Fundamental Optimization Formulation of Diffeomorphic Deformable Registration**

$$\begin{aligned}
 & \min_v \underbrace{Mat(\varphi \circ s, t)}_{\text{Data Match}} + \underbrace{(\lambda)Reg(v)}_{\text{Regularization}}, \\
 & s.t. \underbrace{\frac{\partial \phi(t)}{\partial t} = v(\phi(t)), \phi(0) = Id, \varphi = \phi(1)}_{\text{Constraint}}.
 \end{aligned}$$

- **Deep Propagation on Feature Space *in Sec.2***



Optimization Learning for MIR



- Error-Based Data **Matching** Module

$$u^{k+1} = \mathcal{M}(\varphi^k, f_s^{k+1}, f_t^{k+1}, e^{k+1}; w_{\mathcal{M}^{k+1}}),$$

- Context-based **Regularization** Module

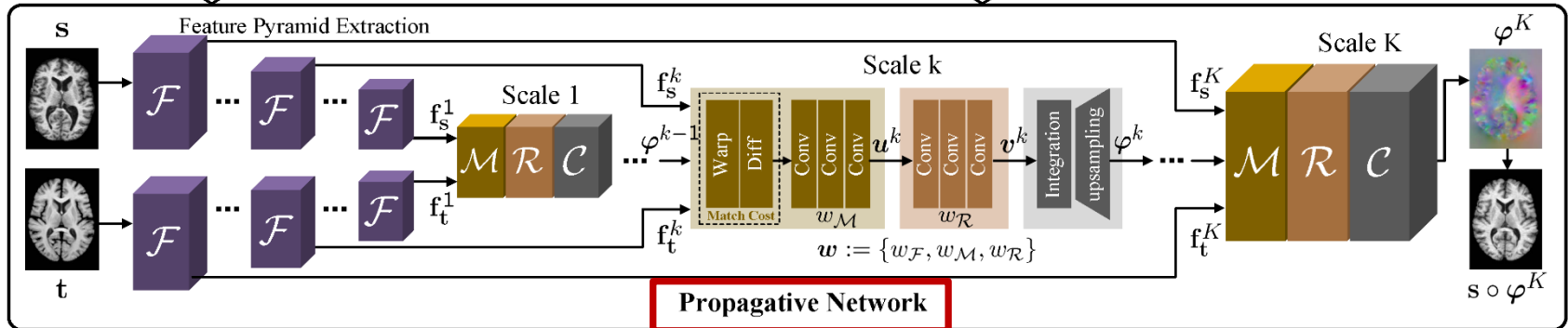
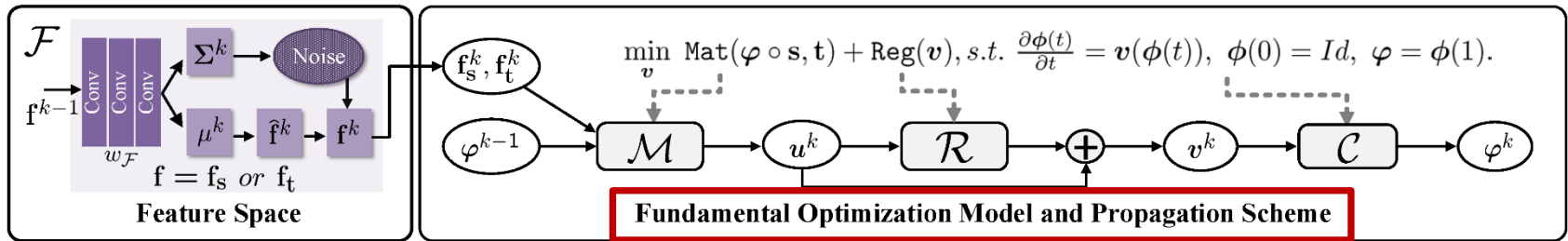
$$v^{k+1} = \mathcal{R}(u^{k+1}; w_{\mathcal{R}^{k+1}}),$$

- **Constraint** Module

$$\varphi^{k+1} = \mathcal{C}(v^{k+1}; w_c).$$

Optimization Learning for MIR

● Learning Registration from Optimization on Feature Space in **Sec.2**

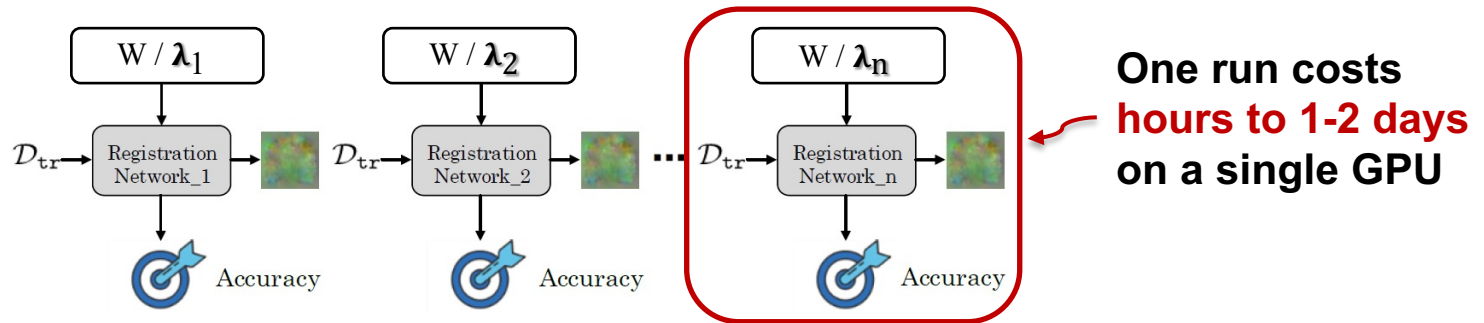


Objective

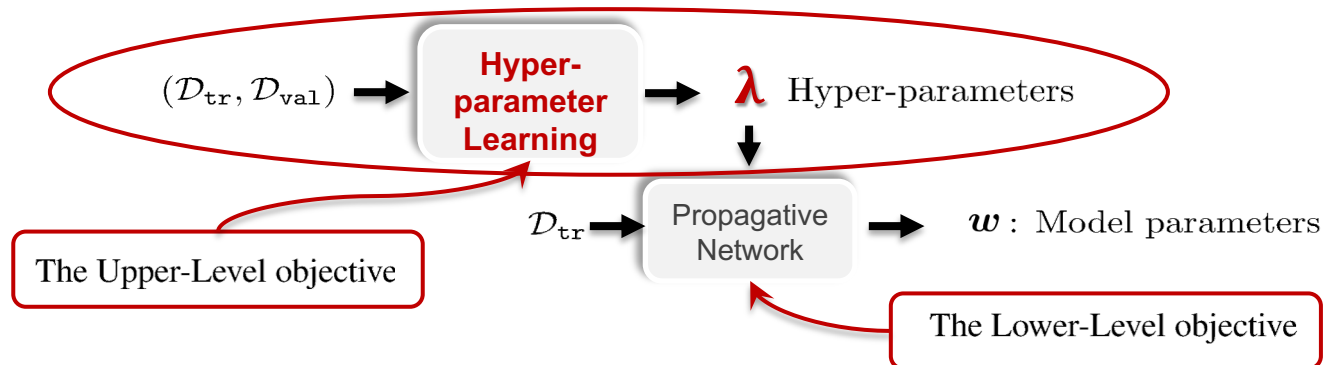
$$l(w(\lambda), s_i, t_i) = \sum_0^K \lambda_{sta}^k \left(l_{KL}(\mu^k, \Sigma^k) + \lambda_{mat} l_{mat}(s_i \circ \varphi^k, t_i) + \lambda_{reg} l_{reg}(v^k) \right)$$

Optimization Learning for MIR

■ Conventional Objective Choosing through Many Training Runs

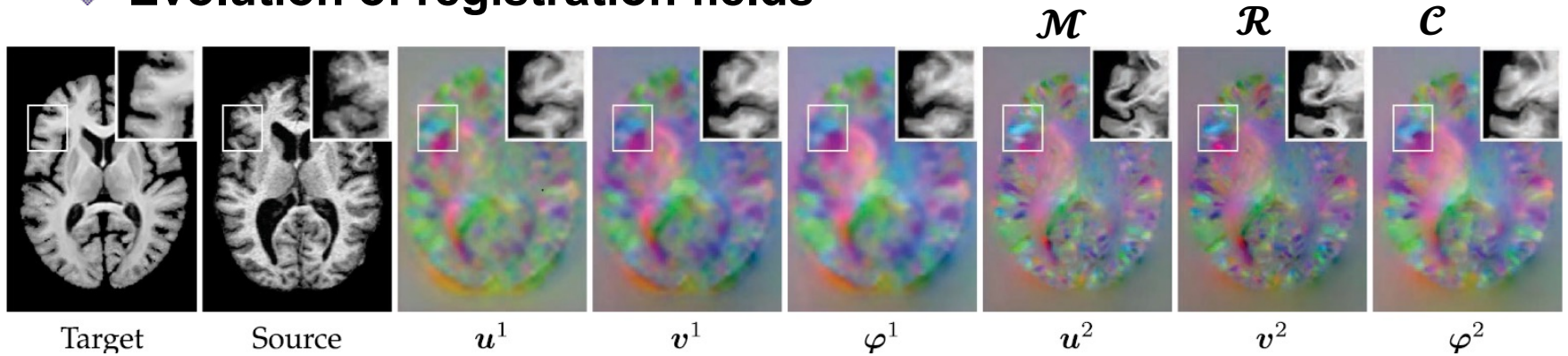


● Bilevel Self-tuned Training for λ

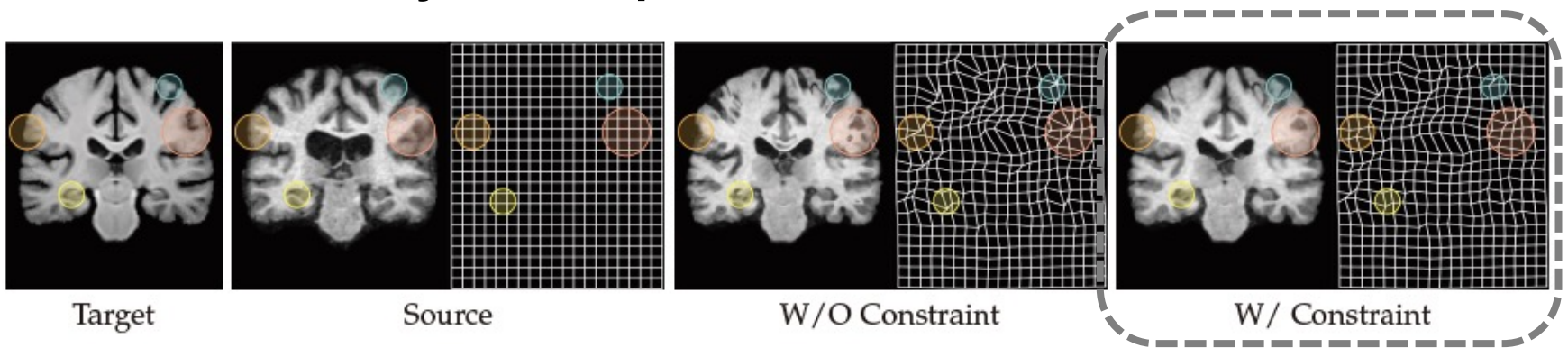


Optimization Learning for MIR

◆ Evolution of registration fields



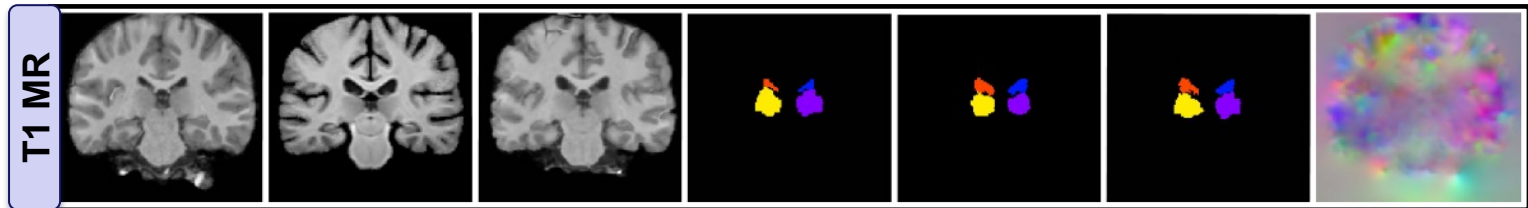
◆ Ablation analysis of explicit constraints



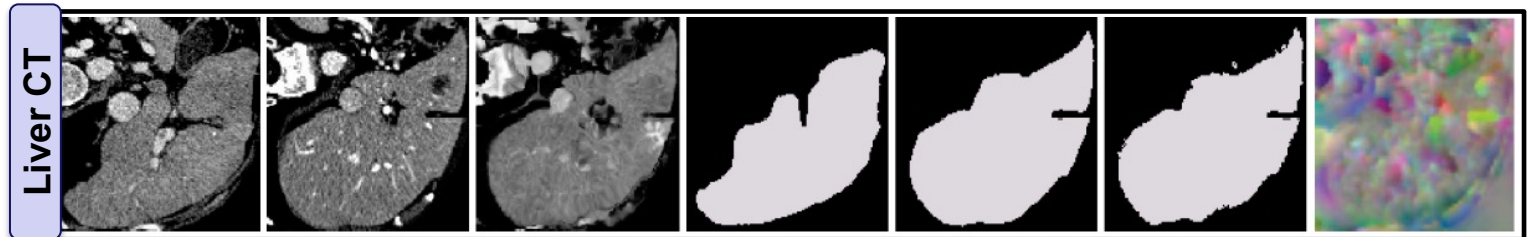
Optimization Learning for MIR

◆ Searched hyperparameters for three tasks

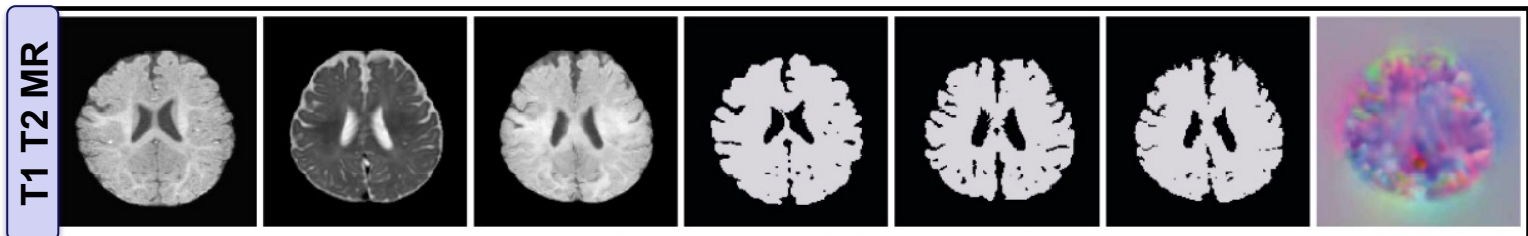
$W / \lambda = 1.6$



$W / \lambda = 1.2$



$W / \lambda = 0.1$

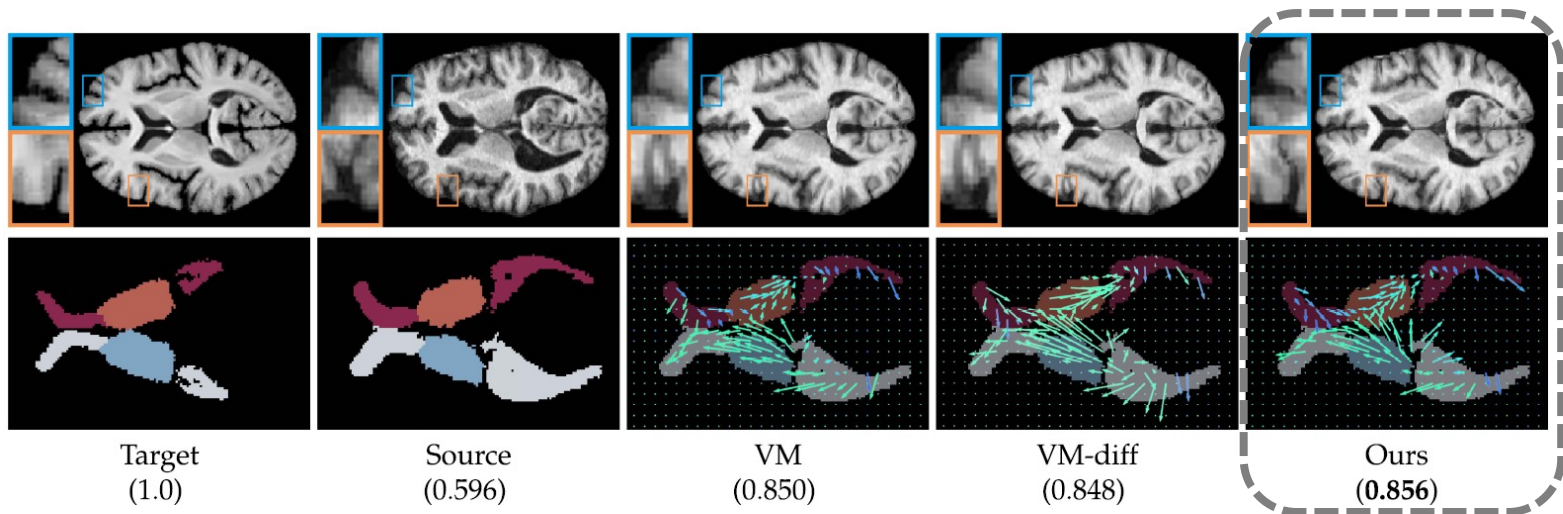
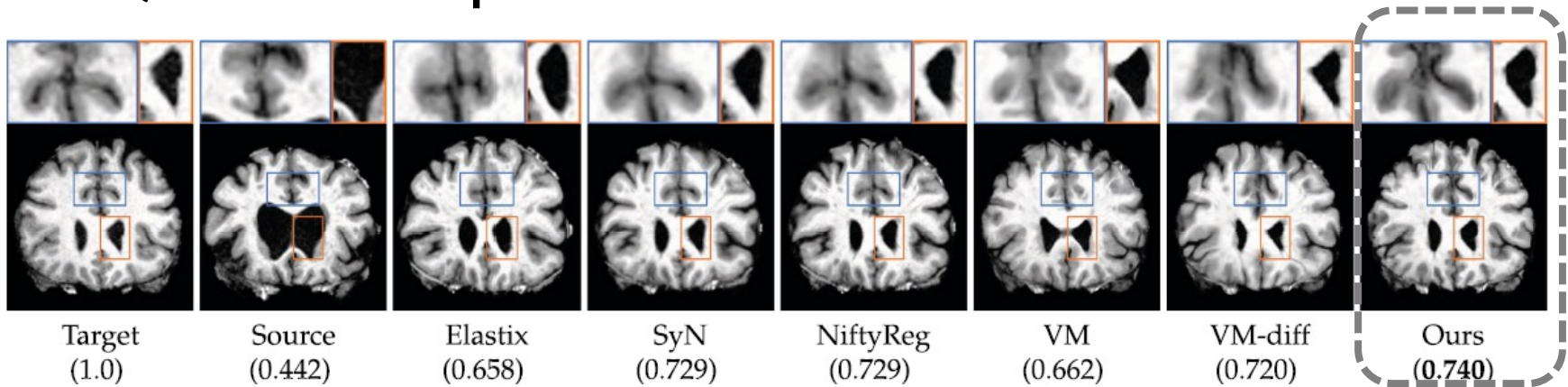


Source Target Warped Sou. Label Tar. Label Warped Label Flow Field

Optimization Learning for MIR

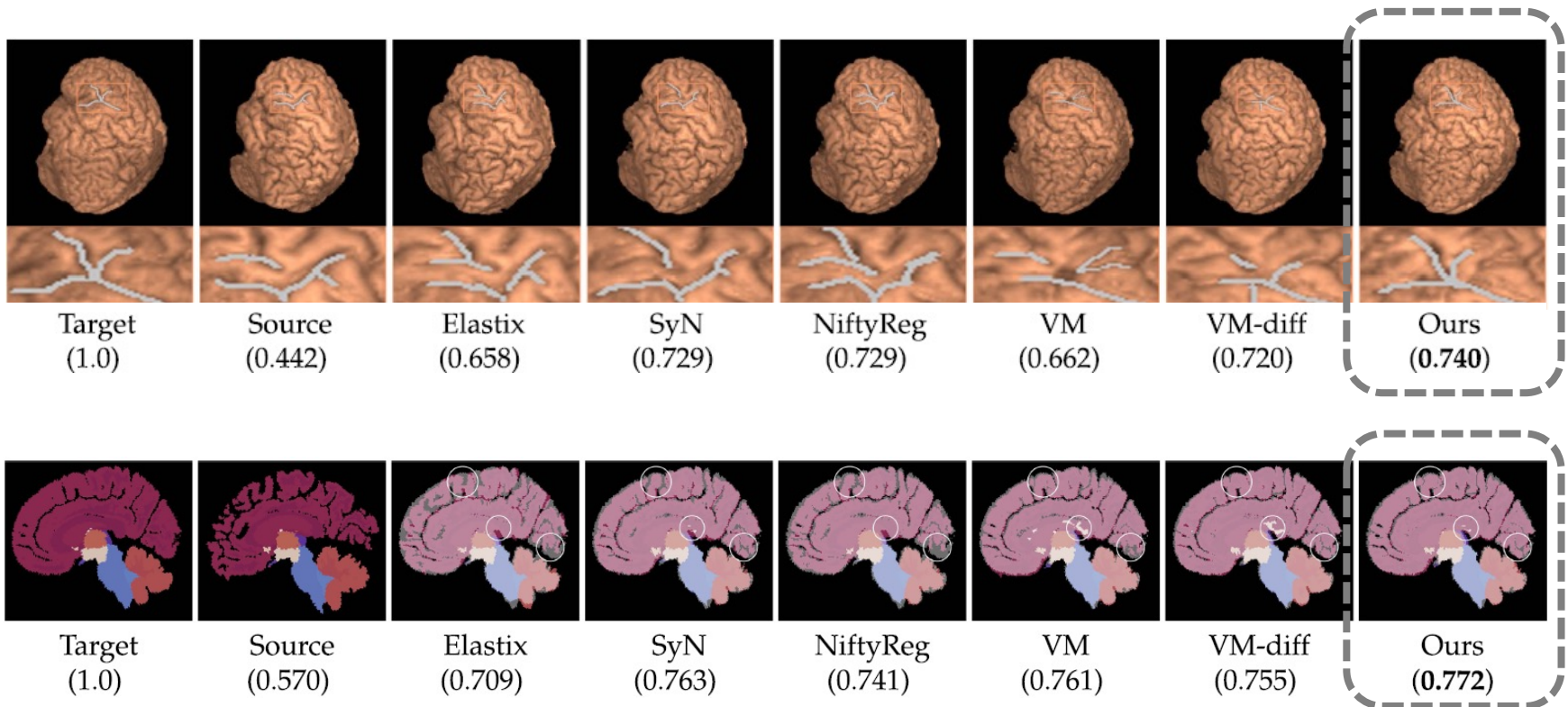


◆ Qualitative comparisons



Optimization Learning for MIR

◆ Qualitative comparisons

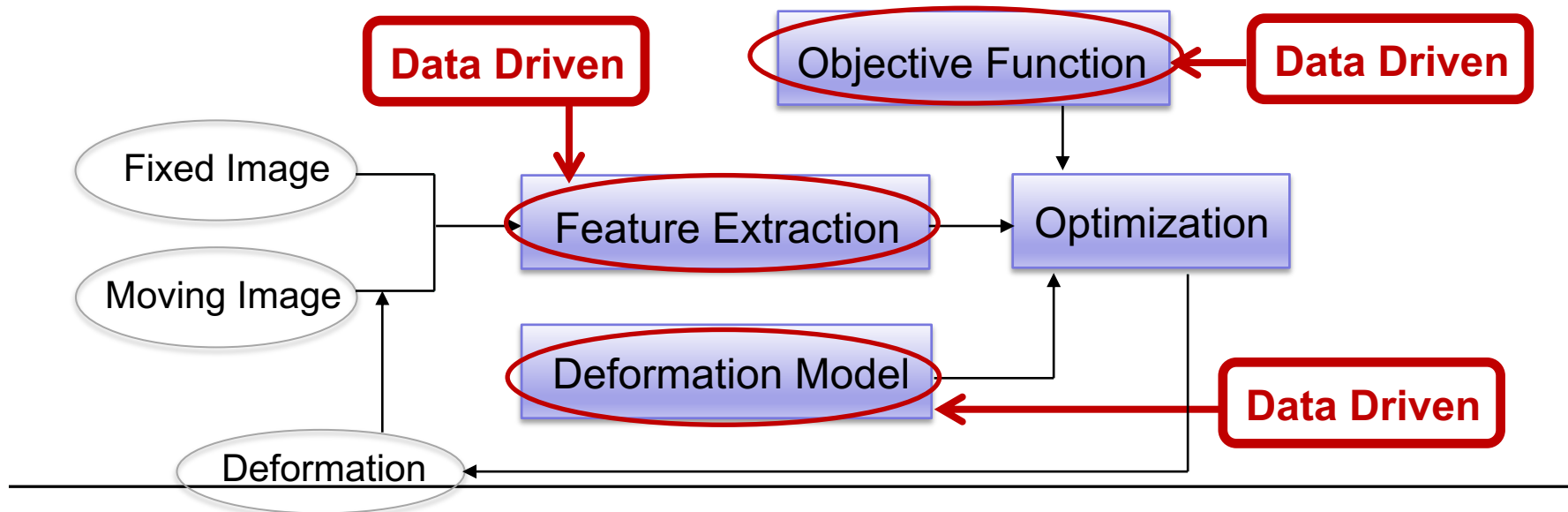




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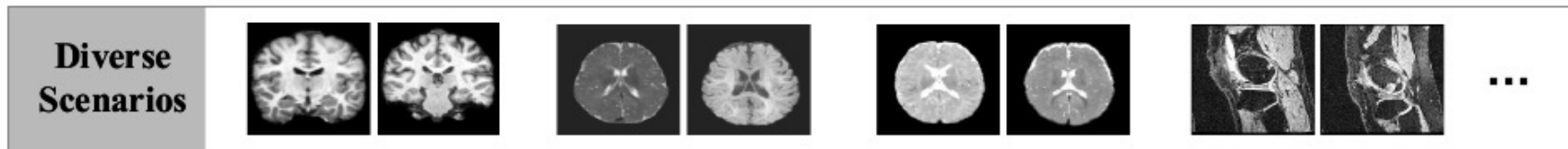
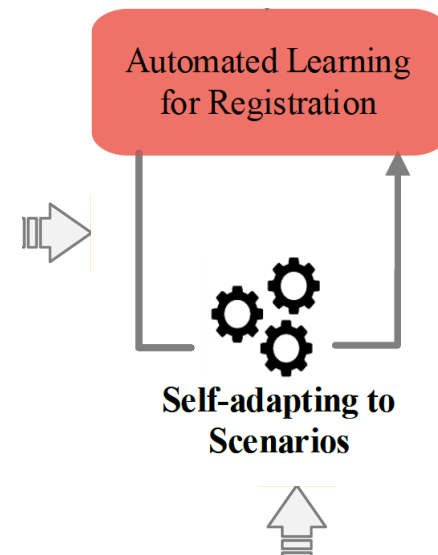


Automated Learning for MIR



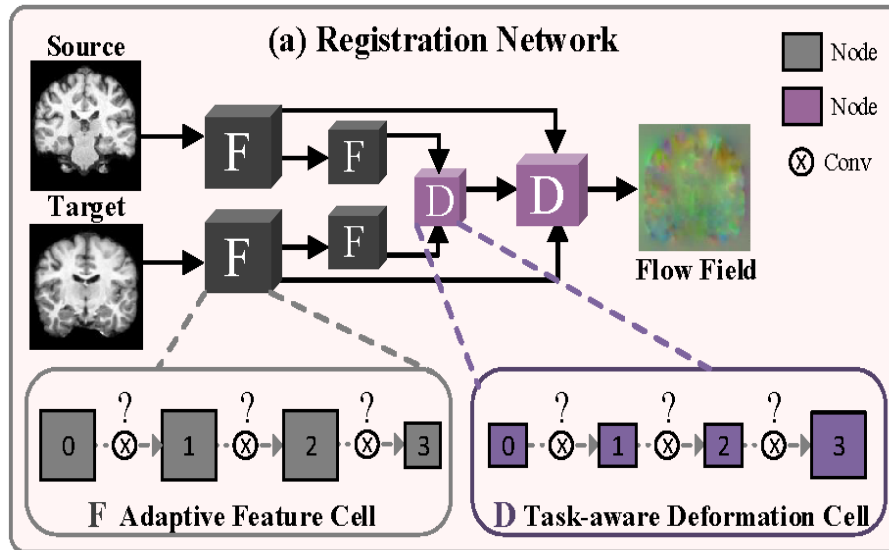
● Triple-level Optimization for AutoReg

$$\begin{aligned} & \min_{\lambda} \mathcal{L}_{val}^{seg}(\lambda, \alpha^*, \omega^*; s, t), \\ \text{s. t. } & \left\{ \begin{array}{l} \alpha^*(\lambda) = \arg \min_{\alpha} \mathcal{L}_{val}^{reg}(\alpha, \omega^*(\alpha); \lambda, s, t), \\ \text{s. t. } \omega^*(\alpha) = \arg \min_{\omega} \mathcal{L}_{tr}^{reg}(\omega; \alpha, \lambda, s, t). \end{array} \right. \end{aligned}$$



Automated Learning for MIR

● Architecture Search: From Hand-design to Search



Search Space

- $1 \times 1 \times 1$ Conv (1-Conv)
- $3 \times 3 \times 3$ Conv (3-Conv)
- $5 \times 5 \times 5$ Conv (5-Conv)
- $3 \times 3 \times 3$ Separable Conv (3-SConv)
- $5 \times 5 \times 5$ Separable Conv (5-SConv)
- $3 \times 3 \times 3$ Dilation Conv (3-DConv)
- $5 \times 5 \times 5$ Dilation Conv (5-DConv)
- $7 \times 7 \times 7$ Dilation Conv (7-DConv)

Automated Learning for MIR



◆ Optimality verification across registration tasks

Method	Brain T1-to-T1	Brain T2-to-T2	Knee T1-to-T1	Brain T2-to-T1
All-1-Conv	0.700 (0.035)	0.610 (0.009)	0.395 (0.110)	0.579 (0.005)
All-3-Conv	0.769 (0.025)	0.636 (0.010)	0.605 (0.131)	0.617 (0.006)
All-7-Conv	0.761 (0.025)	0.610 (0.009)	0.614 (0.091)	0.613 (0.007)
AutoReg	0.778 (0.023)	0.646 (0.010)	0.616 (0.150)	0.622 (0.007)

◆ Computation cost

Strategy	AutoReg + Training	Manual + Training
Runtime	48 + 23 hour	23 * n + 23 hour

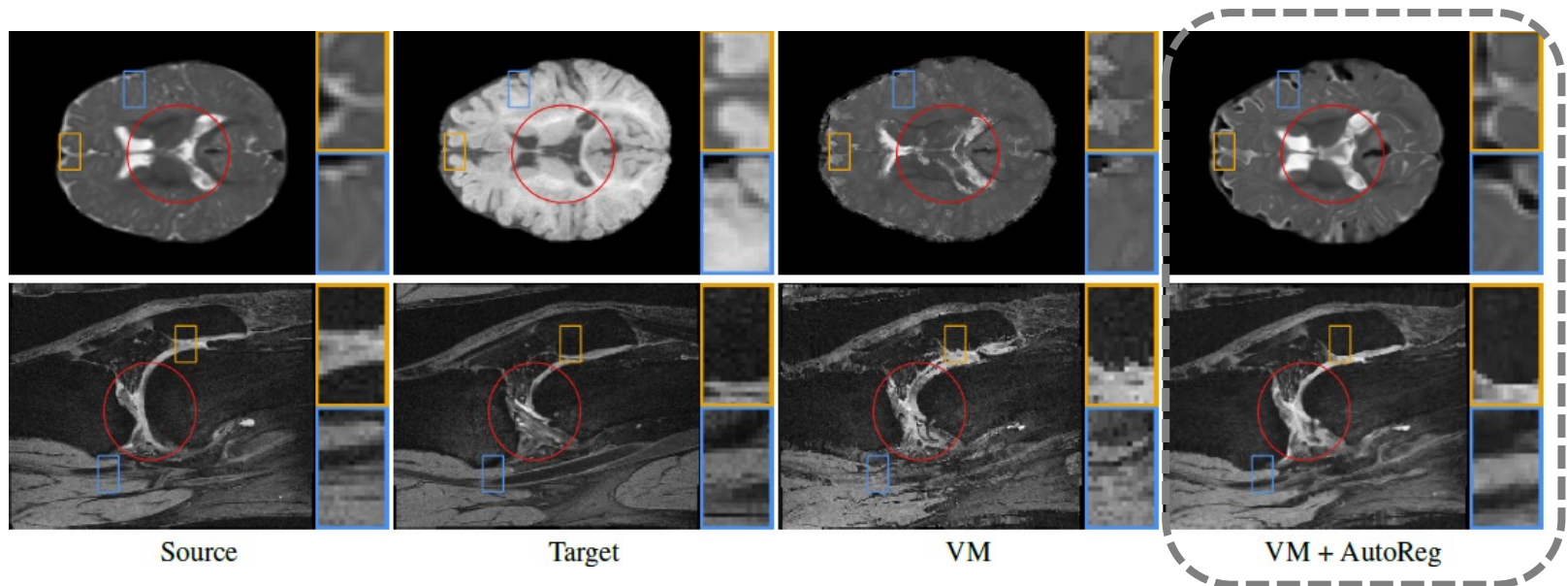
Typically set **larger than 10**

Automated Learning for MIR



◆ Generalizability analysis

Method	Brain T1-to-T1	Brain T2-to-T2	Knee T1-to-T1	Brain T2-to-T1
VM	0.757 (0.035)	0.638 (0.012)	0.440 (0.132)	0.579 (0.013)
VM + AutoReg	0.761 (0.010)	0.640 (0.013)	0.482 (0.151)	0.596 (0.006)



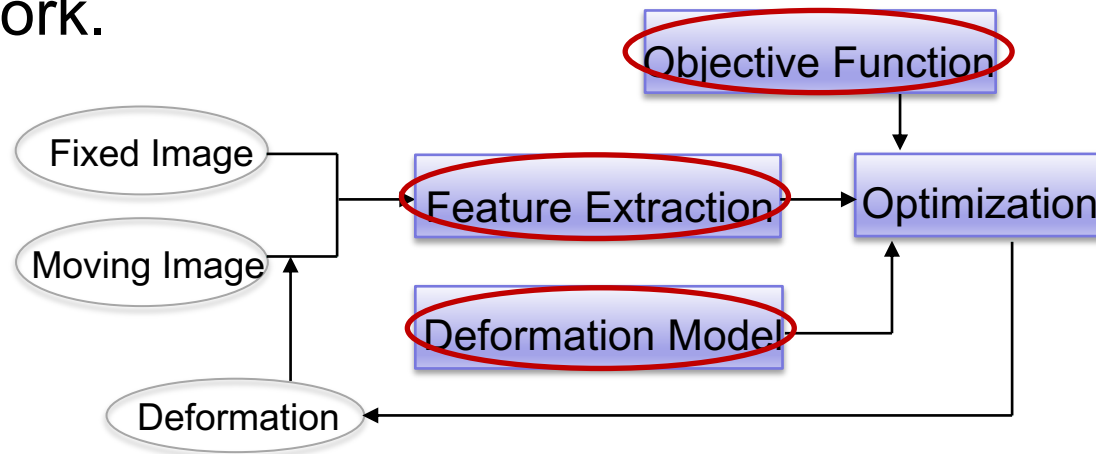


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Summary

- Integrates **deep learning** with **bilevel optimization** and proposes algorithms from **three aspects** of registration framework.



- **Feature learning-based** bi-level optimization model
- Novel similarity measurement, bilevel **self-tuned loss function**
- Automated optimization of the **loss function** and **architecture** of feature/deformation learning modules

Future Work

□ Auto Learning for Registration

$$\begin{aligned} & \min_{\lambda} \mathcal{L}_{val}^{seg}(\lambda, \alpha^*, \omega^*; s, t), \\ \text{s. t. } & \left\{ \begin{array}{l} \alpha^*(\lambda) = \arg \min_{\alpha} \mathcal{L}_{val}^{reg}(\alpha, \omega^*(\alpha); \lambda, s, t), \\ \text{s. t. } \omega^*(\alpha) = \arg \min_{\omega} \mathcal{L}_{tr}^{reg}(\omega; \alpha, \lambda, s, t). \end{array} \right. \end{aligned}$$

Cover other architectural hyperparameters

- network topology that controls the connections among cells
- number of layers and resolution levels
- ...



Acknowledgment

◆ Natural Science Foundation of China

◆ Faculty members

- **Xin Fan**—Professor, Dalian University of Technology
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- **Huang Hao**—Professor, University of Pennsylvania

◆ Students

- **Yuxi Zhang**—Dalian University of Technology
- **Ziyang Li**—Dalian University of Technology

...

Thanks !

