CONTRASTIVE LEARNING FOR CROSS-MODALITY IMAGE REGISTRATION IN BIOMEDICAL IMAGING

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ABSTRACT

Image registration between different imaging modalities (e.g. CT vs MRI, MR vs ultrasound, bright-field vs fluorescence microscopy) is a central problem in biomedical imaging. Due to differences in contrast, noise, appearance and sometimes spatial distortions, conventional intensity- or feature-based registration methods often struggle in cross-modality settings. Contrastive learning—originally developed for representation learning—offers a promising route to learn modality-agnostic features or representations that capture shared anatomical or structural information. In this paper, we review and propose methods by which contrastive learning can be effectively applied for cross-modality image registration. We present a general framework, discuss recent advances, identify challenges, and suggest future directions. We also propose a hypothetical method combining anatomy-aware contrastive loss, region masking, and cross-modal attention to improve registration accuracy on typical biomedical datasets.

Keywords: *biomedical imaging, image registration, contrastive learning, noise.*

1. Introduction

Image registration involves aligning two or more images so that corresponding anatomical or structural points (e.g. organs, tissues) match geometrically. In biomedical imaging, cross-modality registration is particularly important:

- Combining information from different modalities (e.g., CT for bone structure, MRI for soft tissue, ultrasound for real-time imaging).
- Multimodal longitudinal studies, fusion of histology with in vivo imaging, image-guided therapy and surgical navigation.

However, cross-modality registration is difficult because:

Appearance differences: Intensities in CT vs MRI are not directly comparable; texture, shading, and contrast vary widely.

Noise, artifacts and resolution mismatches.

Lack of a shared intensity similarity metric. Many classic registration algorithms depend on e.g. mutual information or other metrics designed for cross-modality similarity — but these may fail when structures are subtle or noise is high.

Contrastive learning has emerged in machine learning as a way to learn representations by contrasting "positive pairs" (similar examples) with "negative pairs" (dissimilar ones). In cross-modality registration, the idea is to learn representations so that images (or patches/features) from different modalities that correspond anatomically map to similar feature vectors, while non-corresponding ones map apart.

2. Background

Image registration

- **Rigid vs deformable registration**: Rigid (translations, rotations) sufficient in some cases; deformable needed when tissues deform.
- **Monomodal vs multimodal registration**: Monomodal (same imaging modality) easier, since intensity relationships are simpler; cross-modality introduces challenges.
- **Similarity metrics** used in classical registration: sum of squared differences (SSD), cross-correlation, mutual information, normalized mutual information, etc.

Contrastive Learning

- **Basic contrastive loss**: Given (x, x^+) positive pair and negatives x^-, encouraging representation of x to be closer to x^+ and farther from negatives. Examples: InfoNCE loss.

- **Self-supervised contrastive learning**: Using data augmentations to generate positives, large amounts of unlabeled data.
- **Contrastive patch or spatial contrastive learning**: Instead of whole image, matching patches (spatial correspondence) which is especially relevant in registration.

Prior work combining cross-modality registration and contrastive learning

Some representative works:

- **CoMIR** (Contrastive Multimodal Image Representation) learns shared dense image representations for two modalities via contrastive loss (InfoNCE), then applies monomodal registration methods on these representations.
- **Cross-modal attention with contrastive pre-training**: For example, MR–TRUS registration using cross-modal attention, where contrastive pretraining helps features become modality-invariant before further training for spatial alignment.
- **Spatial-aware contrastive learning for CT-MRI registration**: Using contrastive loss plus reconstruction loss and region masks to encourage both spatial correspondence and distinctive representation.
- **CBCRnet**: Contrast-Reconstruction tasks guided pretraining for modal-independent features, bidirectional cross-modal attention.

3. A General Framework for Contrastive Learning in Cross-Modality Registration

Here we propose a unified framework, integrating insights from prior work, for applying contrastive learning to cross-modality image registration.

Data Preparation

- **Paired images**: If possible, use images from different modalities that are already approximately aligned or correspond to the same subject (even if not perfectly).
- **Unpaired images**: If true pairs are unavailable, synthetic pairing, or weak pairing (e.g. same organ region, same patient, approximate alignment) can be used.
- **Patch extraction**: Extract patches from corresponding locations for positive pairs; non-corresponding patches serve as negatives.

Network Architecture

- Two (or more) encoders, one per modality, or a shared encoder with adaptation modules.
- Cross-modal attention blocks to allow the model to explicitly learn spatial correspondences between modalities.
- Optional decoders if one wants to reconstruct images, or produce registration transformations (rigid / deformable).

Loss Functions

- **Contrastive loss (e.g. InfoNCE)**: On representations extracted from corresponding patches/images from different modalities.
- **Anatomy-aware or structure-aware contrastive loss**: Encourage alignment of anatomical structures; can use masks or segmentation annotations if available.
- **Reconstruction or translation losses**: In some designs, to ensure features preserve shape / structure across translation.
- **Regularization losses**: Spatial smoothness, deformation regularization for deformable registration, etc.

Training Strategy

- **Pretraining**: Use contrastive learning first to learn modality-invariant or shared structural features.
- **Fine-tuning**: Then train registration network (rigid/deformable) using either supervised (if ground truth deformations available) or unsupervised alignment, possibly using feature similarity in learned representation space.

Evaluation

- Standard registration metrics: Dice similarity coefficient (DSC), target registration error (TRE), Hausdorff distance, mean surface distance, etc.
- Visual inspection of overlays, contours.
- Testing on diverse modalities (e.g. CT/MR, MR/US, microscopy modalities).
- Ablation studies: effect of different losses, attention modules, patch sizes, etc.

4. Proposed Method (Hypothetical/Combined Approach)

This section outlines a hypothetical improvement combining several techniques to address common challenges.

Method Overview

We call the method **Anatomy-Aware Cross-Modal Contrastive Registration (ACCR)**.
The components:

a. **Dual Encoders**: One encoder for each modality. Use of shared weights in early layers to encourage shared structure features; modality-specific layers later.
b. **Cross-Modal Attention Module**: After encoding, cross-attention layers align feature maps across modalities to capture spatial correspondences.
c. **Anatomy-Aware Contrastive Loss**:
    - Use anatomical masks (if available) to generate positive pairs across modalities only in corresponding anatomical regions; ensure negatives are from other regions.
    - Employ patch-wise contrastive loss: matching patches that correspond to same location / anatomical region.
d. **Structure Self-Similarity Loss**: For each image, compute self-similarity of local neighborhoods (e.g. for a patch, the similarity with neighboring patches), and enforce that the representation preserves structural self-similarity across modalities.
e. **Deformable Registration Module**: On top of representations, a registration module predicts transformation (rigid or deformable) that aligns the floating image to the fixed.

Training Pipeline

- Stage 1: Pretrain encoders + attention + contrastive and self-similarity losses using paired or weakly paired images.
- Stage 2: Introduce registration module; jointly train with representation fixed or finetuned.
- Stage 3: If annotations available, optionally fine-tune using supervised losses.

5. Challenges

Even with this framework, there are several challenges:

- **Availability of paired data**: Many datasets do not have perfectly aligned cross-modality images. Weak supervision or synthetic pairing may help, but may introduce errors.
- **Scale and resolution differences**: Modalities may have different spatial resolutions, field-of-view, or distortions.
- **Anatomical deformations**: Nonlinear deformations (e.g. breathing motion, tissue deformation) complicate matching.
- **Inter-modality inconsistencies**: Some structures visible in one modality may not be visible in another; appearance may differ extremely.
- **Negative sampling** in contrastive learning: choosing negatives that are informative is critical; false negatives (i.e. patches that look different but correspond anatomically) can degrade learning.
- **Computational cost**: Patch-wise contrastive learning, deformable registration, large 3D volumes — demands on memory and compute are high.

6. Experimental Design

To validate ACCR, one might design experiments as follows:

Datasets:

- MR-CT scans from abdominal imaging.
- MR-Ultrasound scans (e.g. prostate).
- Microscopy modalities (bright-field vs fluorescence / SHG etc).

Baseline Methods:

- Classical registration (mutual information, cross correlation).
- CoMIR.
- Cross-modal attention methods.
- CBCRnet.

Evaluation Metrics:

- Dice coefficient on segmented structures.
- TRE measured on landmark points.
- Hausdorff distance.
- Run time and memory usage.

Ablation Studies:

- With vs without attention module.
- With vs without structure self-similarity loss.
- Different patch sizes; different negative sampling strategies.

Qualitative Analysis:

- Overlayed images before/after registration.
- Heatmaps of attention / feature correspondence.

9. Conclusion

Contrastive learning offers a powerful tool for bridging modality gaps in biomedical image registration by learning shared, structure-aware feature representations. When combined with attention mechanisms, anatomical awareness, and well-designed loss functions, such methods promise to substantially improve registration performance over classical or purely intensity-based methods. Continued progress will depend on better data (especially aligned or weakly aligned cross-modality data), clever representation learning, and scalable architectures.

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