

# Registration of Multimodal Microscopy Images using CoMIR – Learned Structural Image Representations

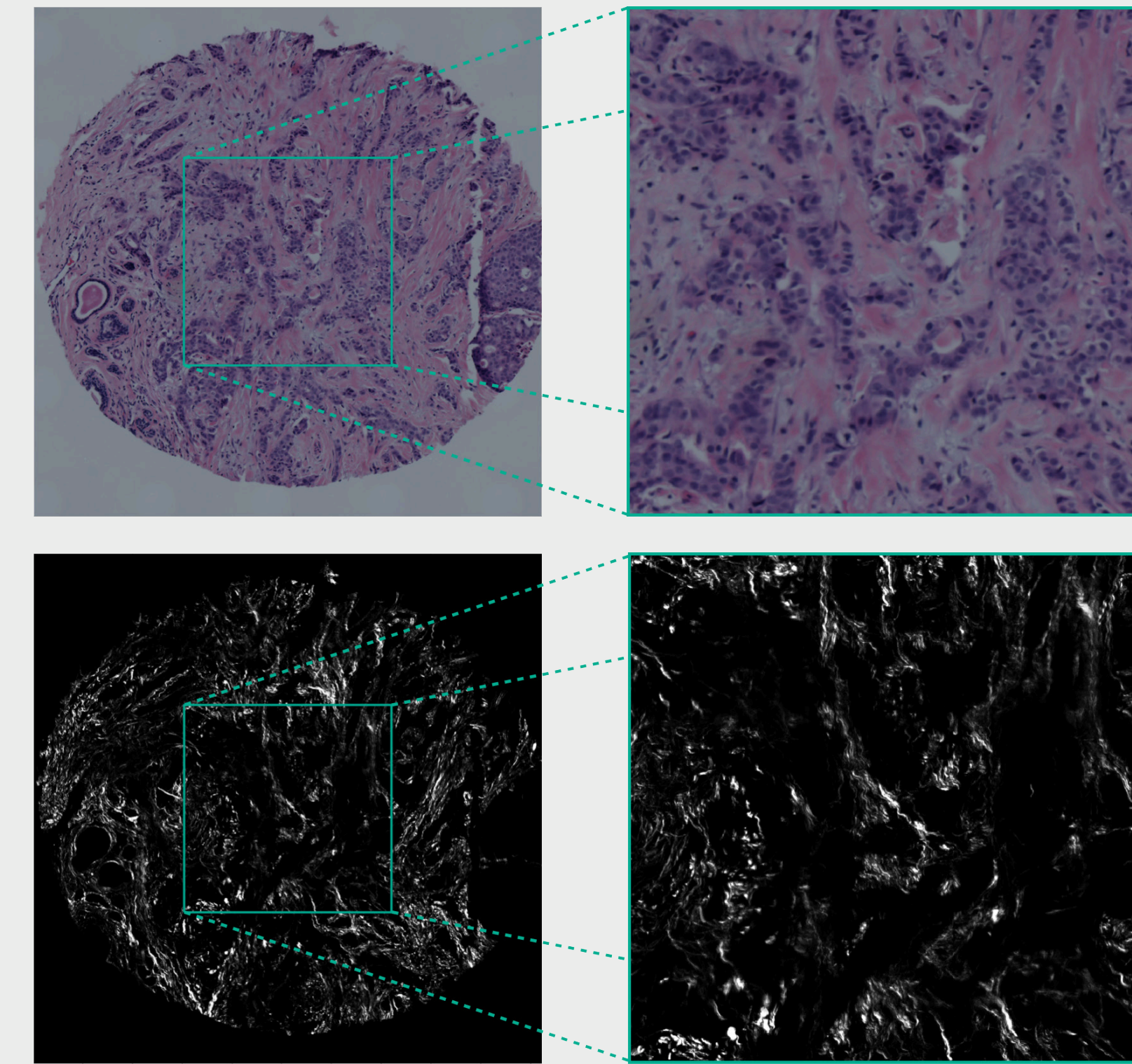


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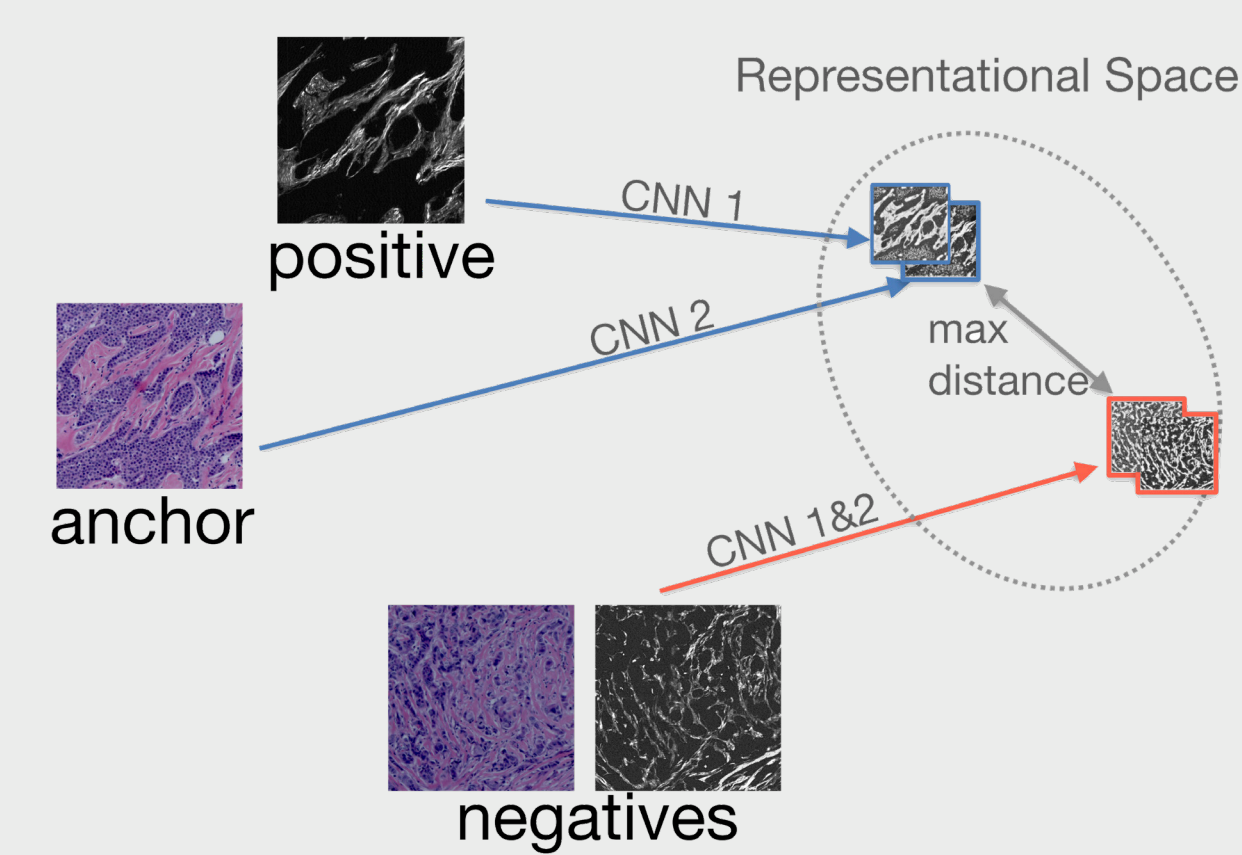
## Introduction

- Combining information of multiple modalities for one specimen can shed light on properties not detectable by only one modality as they can provide complementary signals.
- Multimodal Registration can be extremely challenging if the appearance or signal expression density differs greatly between the modalities, as is the case for brightfield microscopy (BF) and second harmonic generation (SHG).
- We have developed contrastive learning based on InfoNCE [2] to learn representations from different modalities, called CoMIRs [1], which are visually similar.
- These image-like, dense representations can be successfully registered by monomodal rigid registration methods, e.g.  $\alpha$ -AMD (intensity-based, [3]) or using SIFT (feature-based, [4]).
- No data-specific information is incorporated in the learning, i.e. the method is modality independent and can be applied to other imaging modalities than BF and SHG.
- Very little aligned training data is required, for modalities which share sufficient structural similarities, the required aligned training data can be as little as one image pair.



**Fig. 1:** Patches which are to be registered (available at [5]), cut from TMA cores captured by BF and SHG [6]. In our performance evaluation random rotations by  $\pm 30^\circ$  and random translations by  $\pm 100$ px were applied to the patches of  $834 \times 834$ px in size.

## Contrastive Learning

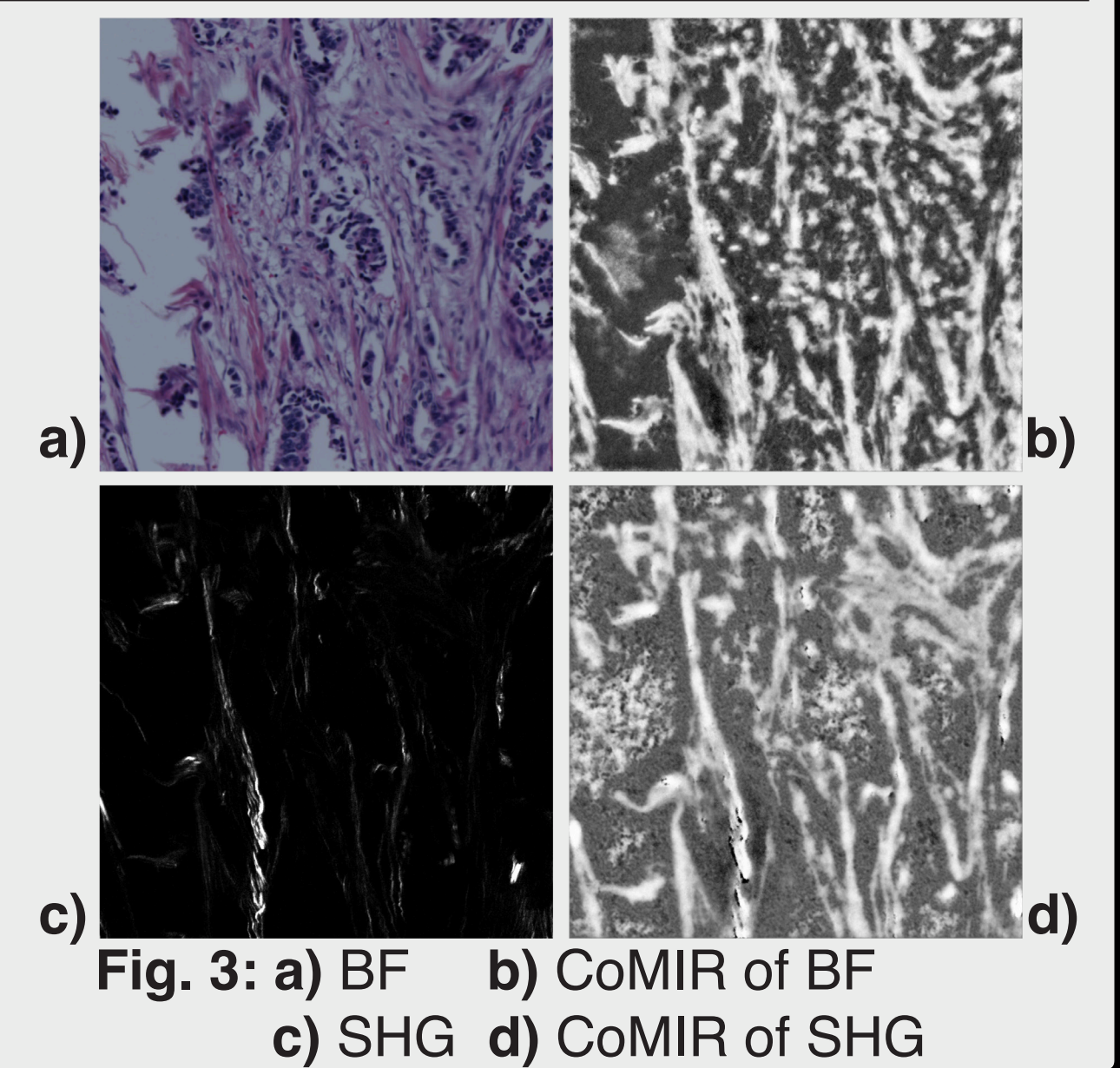


**Fig. 2:** Through contrastive learning our method produces abstract representations which are very similar for all input modalities.

- A randomly cropped patch in one modality serves as an anchor. Its corresponding patch in the other modality acts as a positive. Any other patch of any modality serves as a negative.
- Two CNNs, sharing no weights, only connected by the loss function, learn dense representations by maximizing the distance between the anchor and the negatives, as well as minimizing the distance between the anchor and the positive.

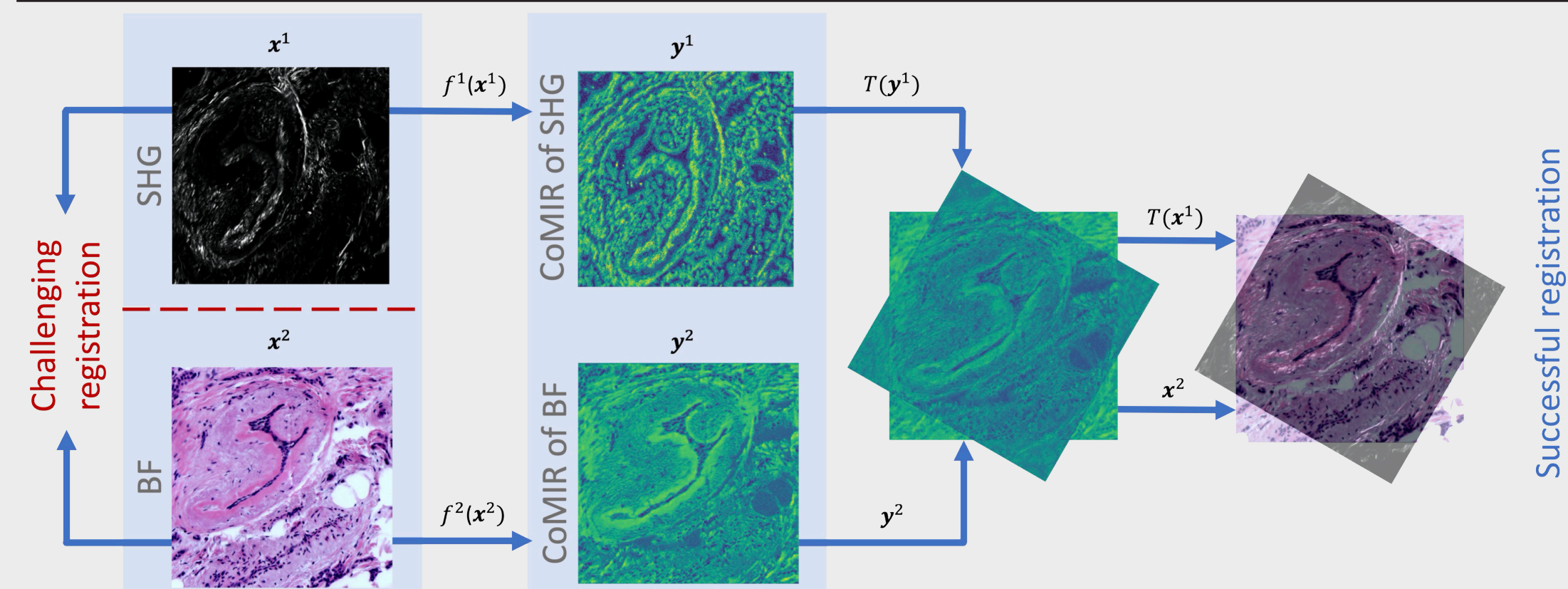
## CoMIRs

- We require certain properties of the representations, such as rotational equivariance and similar intensities, which can be realized through the loss function without any additional hyperparameters.
- The appearance of CoMIRs depends on the choice of similarity function; MSE yielded the best results.
- The number of channels for the CoMIRs can be chosen; single channel CoMIRs expedite registration.



**Fig. 3:** a) BF b) CoMIR of BF c) SHG d) CoMIR of SHG

## Registration of CoMIRs

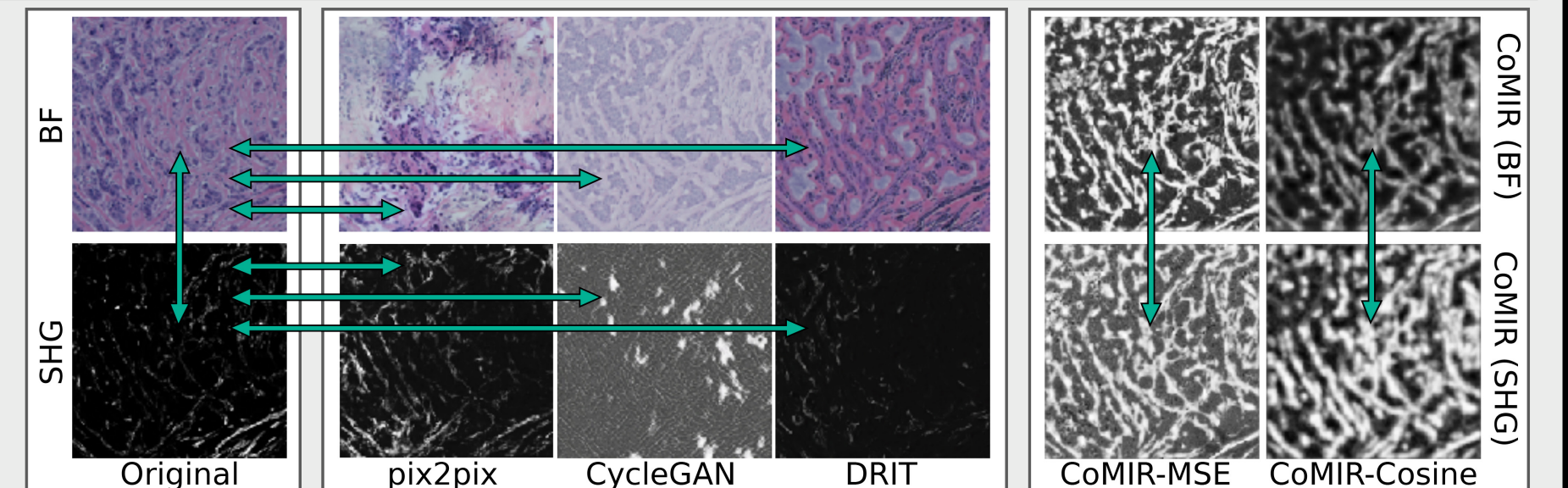


**Fig. 4:** The transformation found for the CoMIRs is applied to the original modalities to achieve multimodal registration.

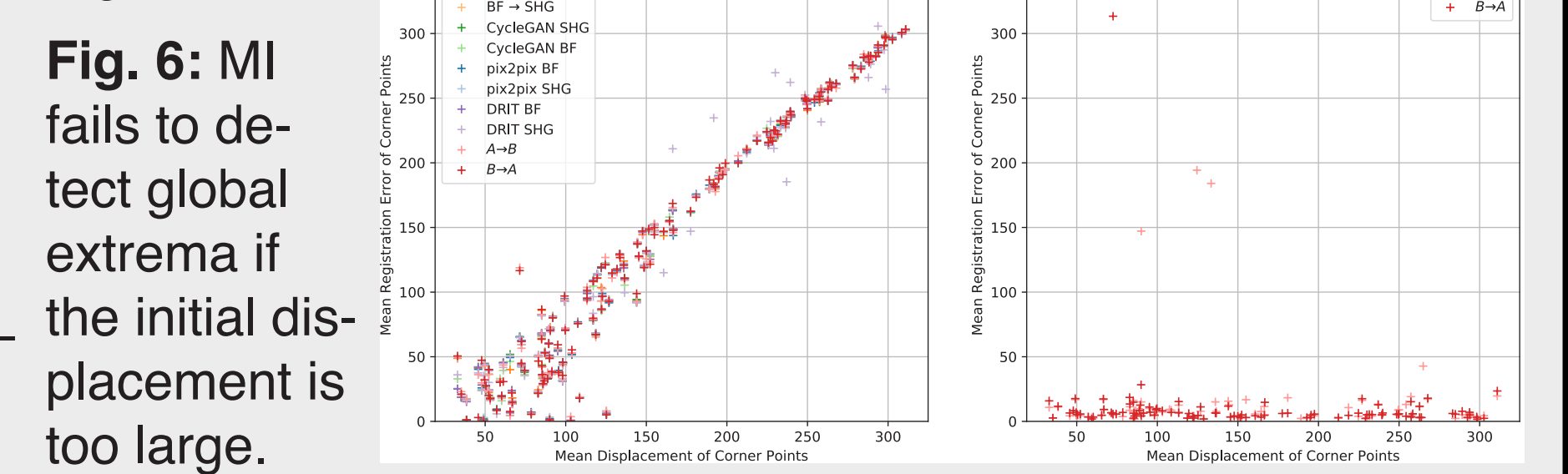
- CoMIRs can be registered by common monomodal methods based on their intensities (e.g.  $\alpha$ -AMD [3]) or by feature-based methods (e.g. using SIFT [4]).
- A transformation found for CoMIRs can be applied to original modalities and solve the multimodal registration.

## Competing Methods

- CurveAlign: registers BF and SHG, using modality specific information and mutual information (MI) [6].
- GAN-based Image Translation methods: pix2pix, CycleGAN, DRIT. The resulting "fake" modalities do not qualify for intensity- or feature based monomodal registration methods.

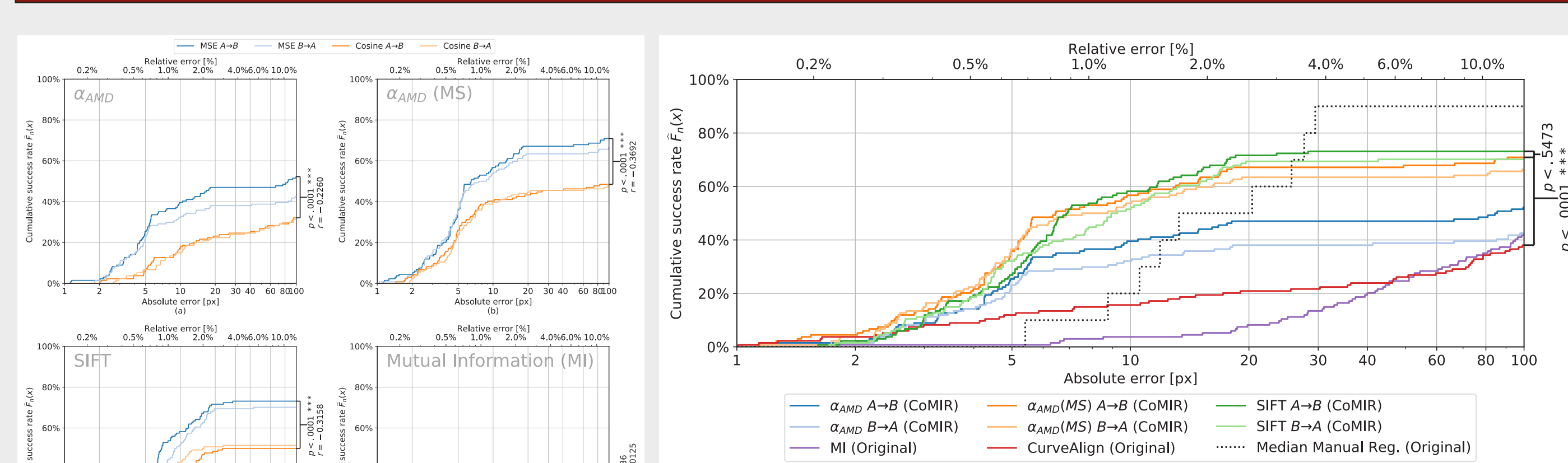


**Fig. 5:** Image translation methods to transform BF and SHG into one common modality. Arrows indicate resulting pairs for registration.



**Fig. 6:** MI fails to detect global extrema if the initial displacement is too large.

## Results and Conclusions



**Fig. 7:** Success rate as a function of tolerated residual error of the CoMIRs based on MSE.

- CoMIRs extract shared content in multimodal images and enable multimodal registration by reducing the problem to a monomodal one.
- CoMIRs combined with monomodal intensity- and feature-based registration methods significantly outperform multimodal registration by MI as well as a state-of-the-art data-specific approach. Best results were obtained using SIFT.
- CoMIRs contain more valuable information than GAN generated images obtained by image-to-image translation from one modality to the other.
- Feature-based registration does not depend on the initial displacement of the images as is the case for MI-based approaches.

## References and Code

Code available at <https://github.com/MIDA-group/CoMIR>

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