DEEPREG: A DEEP LEARNING TOOLKIT
FOR MEDICAL IMAGE REGISTRATION

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Abstract

DeepReg (https://github.com/DeepRegNet/DeepReg) is a community-supported open-source toolkit for research and education in medical image registration using deep learning.

1 Summary

Image fusion is a fundamental task in medical image analysis and computer-assisted intervention. Medical image registration, computational algorithms that align different images together [1], has in recent years turned the research attention towards deep learning. Indeed, the representation ability to learn from population data with deep neural networks has opened new possibilities for improving registration generalisability by mitigating difficulties in designing hand-engineered image features and similarity measures for many real-world clinical applications [2, 3]. In addition, its fast inference can substantially accelerate registration execution for time-critical tasks.

DeepReg is a Python package using TensorFlow [4] that implements multiple registration algorithms and a set of predefined dataset loaders, supporting both labelled- and unlabelled data. DeepReg also provides command-line tool options that enable basic and advanced functionalities for model training, prediction and image warping. These implementations, together with their documentation, tutorials and demos, aim to simplify workflows for prototyping and developing novel methodology, utilising latest development and accessing quality research advances. DeepReg is unit tested and a set of customised contributor guidelines are provided to facilitate community contributions.

A submission to the MICCAI Educational Challenge has utilised the DeepReg code and demos to explore the link between classical algorithms and deep-learning-based methods [5], while a recently published research work investigated temporal changes in prostate cancer imaging, by using a longitudinal registration adapted from the DeepReg code [6].

2 Statement of need

Currently, popular packages focusing on deep learning methods for medical imaging, such as NiftyNet [7] and MONAI (https://monai.io/), do not support image registration. The existing open-sourced registration projects either implement specific published algorithms without automated testing, such as the VoxelMorph [8], or focus on classical methods, such as NiftiReg [9], SimpleElastix [10] and AirLab [11]. Therefore an open-sourced project focusing on image registration with deep learning is much needed for general research and education purposes.
3 Implementation

DeepReg implements a framework for unsupervised learning \cite{12, 8}, weakly-supervised learning \cite{13, 14} and their combinations and variants, e.g. \cite{15}. Many options are included for major components of these approaches, such as different image- and label dissimilarity functions, transformation models \cite{16, 17, 1}, deformation regularisation \cite{18} and different neural network architectures \cite{14, 19, 20}. Details of the implemented methods are described in the documentation. The provided dataset loaders adopt staged random sampling strategy to ensure unbiased learning from groups, images and labels \cite{14, 6}. These algorithmic components together with the flexible dataset loaders are building blocks of many other registration tasks, such as group-wise registration and morphological template construction \cite{21, 22, 23}.

4 DeepReg Demos

In addition to the tutorials and documentation, DeepReg provides a collection of demonstrations, DeepReg Demos, using open-accessible data with real-world clinical applications.

4.1 Paired images

Many clinical applications for tracking organ motion and other temporal changes require intra-subject single-modality image registration. Registering lung CT images for the same patient, acquired at expiratory and inspiratory phases \cite{24}, is such an example of both unsupervised (without labels) and combined supervision (trained with additional label dissimilarity based on anatomical segmentation). Furthermore, registering prostate MR, acquired before surgery, and intra-operative ultrasound images is an example of weakly-supervised learning for multimodal image registration \cite{14}. Another DeepReg Demo illustrates MR-to-ultrasound image registration is to track tissue deformation and brain tumour resection during neurosurgery \cite{25}.

4.2 Unpaired images

Unpaired images are found in applications such as single-modality inter-subject registration. One demo registers different brain MR images from different subjects \cite{26}, fundamental to population studies. Two other applications align unpaired inter-subject CT images for lung \cite{24} and abdominal organs \cite{27}. Additionally, the support for cross-validation in DeepReg has been included in a demo, which registers 3D ultrasound images from different prostate cancer patients.

4.3 Grouped images

Unpaired images may also be grouped in applications such as single-modality intra-subject registration. In this case, each subject has multiple images acquired, for instance, at two or more time points. For demonstration, multi-sequence cardiac MR images, acquired from myocardial infarction patients \cite{28}, are registered, where multiple images within each subject are considered as grouped images. Prostate longitudinal MR registration is proposed to track the cancer progression during active surveillance programme \cite{6}. Using segmentation from this application, another demo application illustrates aligning intra-patient prostate gland masks - also an example of feature-based registration based on deep learning.

5 Conclusion

DeepReg provides a collection of deep learning algorithms and dataset loaders to train image registration networks, which provides a reference of basic functionalities. In its permissible open-source format, DeepReg not only provides a tool for scientific research and higher education, but also welcomes contributions from wider communities.

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References

[1] Derek LG Hill, Philipp G Batchelor, Mark Holden, and David J Hawkes. Medical image registration. *Physics in medicine & biology*, 46(3):R1, 2001.

[2] Grant Haskins, Uwe Kruger, and Pingkun Yan. Deep learning in medical image registration: a survey. *Machine Vision and Applications*, 31(1):8, 2020.

[3] Yabo Fu, Yang Lei, Tonghe Wang, Walter J Curran, Tian Liu, and Xiaofeng Yang. Deep learning in medical image registration: a review. *Physics in Medicine & Biology*, 2020.

[4] Martín Abadi, Ashish Agarwal, Paul Barham, Eugene Brevdo, Zhifeng Chen, Craig Citro, Greg S. Corrado, Andy Davis, Jeffrey Dean, Matthieu Devin, Sanjay Ghemawat, Ian Goodfellow, Andrew Harp, Geoffrey Irving, Michael Isard, Yangqing Jia, Rafal Jozefowicz, Lukasz Kaiser, Manjunath Kudlur, Josh Levenberg, Dandelion Mané, Rajat Monga, Sherry Moore, Derek Murray, Chris Olah, Mike Schuster, Jonathon Shlens, Benoit Steiner, Ilya Sutskever, Kunal Talwar, Paul Tucker, Vincent Vanhoucke, Viçay Vasudevan, Fernanda Viégas, Oriol Vinyals, Pete Warden, Martin Wattenberg, Martin Wicke, Yuan Yu, and Xiaoqiang Zheng. TensorFlow: Large-scale machine learning on heterogeneous systems, 2015. Software available from tensorflow.org.

[5] Nina Montana Brown, Yunguan Fu, Shaheer U. Saeed, Adrià Casamitjana, Zachary M. C. Baum, Rémi Delaunay, Qianye Yang, Alexander Grimwood, Zhe Min, Ester Bonmati, Wasser J Curran, Tian Liu, and Xiaofeng Yang. Introduction to medical image registration with deepreg, between old and new. 2020.

[6] Qianye Yang, Yunguan Fu, Francesco Giganti, Nooshin Ghavami, Qingchao Chen, J. Alison Noble, Tom Vercauteren, Dean Barratt, and Yipeng Hu. Longitudinal image registration with temporal-order and subject-specificity discrimination, 2020.

[7] Eli Gibson, Wenqi Li, Carole Sudre, Lucas Fidon, Dzhoshkun I Shakir, Guotai Wang, Zach Eaton-Rosen, Robert Gray, Tom Doel, Yipeng Hu, et al. Niftynet: a deep-learning platform for medical imaging. *Computer methods and programs in biomedicine*, 158:113–284, 2018.

[8] Guha Balakrishnan, Amy Zhao, Mert R Sabuncu, John Guttag, and Adrian V Dalca. Voxelmorp: a learning framework for deformable medical image registration. *IEEE transactions on medical imaging*, 38(8):1788–1800, 2019.

[9] Marc Modat, Gerard R Ridgway, Zeike A Taylor, Manja Lehmann, Josephine Barnes, David J Hawkes, Nick C Fox, and Sébastien Ourselin. Fast free-form deformation using graphics processing units. *Computer methods and programs in biomedicine*, 98(3):278–284, 2010.

[10] Kasper Marstal, Floris Berendsen, Marius Staring, and Stefan Klein. Simpleelastix: A user-friendly, multi-lingual library for medical image registration. pages 134–142, 2016.

[11] Robin Sandkühler, Christoph Jud, Simon Andermatt, and Philippe C Cattin. Airlab: autograd image registration laboratory. *arXiv preprint arXiv:1806.09907*, 2018.

[12] Bob D de Vos, Floris F Berendsen, Max A Viergever, Hessam Sokooti, Marius Staring, and Ivana Egum. A deep learning framework for unsupervised affine and deformable image registration. *Medical image analysis*, 52:128–143, 2019.

[13] Yipeng Hu, Marc Modat, Eli Gibson, Nooshin Ghavami, Ester Bonmati, Caroline M Moore, Mark Emberton, J Alison Noble, Dean C Barratt, and Tom Vercauteren. Label-driven weakly-supervised learning for multimodal deformable image registration. In *2018 IEEE 15th International Symposium on Biomedical Imaging (ISBI 2018)*, pages 1070–1074. IEEE, 2018.

[14] Yipeng Hu, Marc Modat, Eli Gibson, Wenqi Li, Nooshin Ghavami, Ester Bonmati, Guotai Wang, Steven Bandula, Caroline M Moore, Mark Emberton, et al. Weakly-supervised convolutional neural networks for multimodal image registration. *Medical image analysis*, 49:1–13, 2018.

[15] Yipeng Hu, Eli Gibson, Dean C Barratt, Mark Emberton, J Alison Noble, and Tom Vercauteren. Conditional segmentation in lieu of image registration. In *International Conference on Medical Image Computing and Computer-Assisted Intervention*, pages 401–409. Springer, 2019.

[16] John Ashburner. A fast diffeomorphic image registration algorithm. *Neuroimage*, 38(1):95–113, 2007.

[17] Tom Vercauteren, Xavier Pennec, Aymeric Perchant, and Nicholas Ayache. Diffeomorphic demons: Efficient non-parametric image registration. *NeuroImage*, 45(1):S61–S72, 2009.
[18] Daniel Rueckert, Luke I Sonoda, Carmel Hayes, Derek LG Hill, Martin O Leach, and David J Hawkes. Non-rigid registration using free-form deformations: application to breast mr images. *IEEE transactions on medical imaging*, 18(8):712–721, 1999.

[19] Kaiming He, Xiangyu Zhang, Shaoqing Ren, and Jian Sun. Deep residual learning for image recognition. In *Proceedings of the IEEE conference on computer vision and pattern recognition*, pages 770–778, 2016.

[20] Karen Simonyan and Andrew Zisserman. Very deep convolutional networks for large-scale image recognition. *arXiv preprint arXiv:1409.1556*, 2014.

[21] Adrian Dalca, Marianne Rakic, John Guttag, and Mert Sabuncu. Learning conditional deformable templates with convolutional networks. In *Advances in neural information processing systems*, pages 806–818, 2019.

[22] Hanna Siebert and Mattias P Heinrich. Deep groupwise registration of mri using deforming autoencoders. In *Bildverarbeitung für die Medizin 2020*, pages 236–241. Springer, 2020.

[23] Xinzhe Luo and Xiahai Zhuang. Mvmm-regnet: A new image registration framework based on multivariate mixture model and neural network estimation. *arXiv preprint arXiv:2006.15573*, 2020.

[24] Alessa Hering, Keelin Murphy, and Bram van Ginneken. Lean2Reg Challenge: CT Lung Registration - Training Data, May 2020.

[25] Yiming Xiao, Maryse Fortin, Geirmund Unsgård, Hassan Rivaz, and Ingerid Reinertsen. Retrospective evaluation of cerebral tumors (resect): A clinical database of pre-operative mri and intra-operative ultrasound in low-grade glioma surgeries. *Medical physics*, 44(7):3875–3882, 2017.

[26] Amber L Simpson, Michela Antonelli, Spyridon Bakas, Michel Bilello, Keyvan Farahani, Bram Van Ginneken, Annette Kopp-Schneider, Bennett A Landman, Geert Litjens, Bjoern Menze, et al. A large annotated medical image dataset for the development and evaluation of segmentation algorithms. *arXiv preprint arXiv:1902.09063*, 2019.

[27] Adrian Dalca, Yipeng Hu, Tom Vercauteren, Mattias Heinrich, Lasse Hansen, Marc Modat, Bob de Vos, Yiming Xiao, Hassan Rivaz, Matthieu Chabanas, Ingerid Reinertsen, Bennett Landman, Jorge Cardoso, Bram van Ginneken, Alessa Hering, and Keelin Murphy. Learn2reg - the challenge, March 2020.

[28] Xiahai Zhuang, Jiahang Xu, Xinzhe Luo, Chen Chen, Cheng Ouyang, Daniel Rueckert, Victor M Campello, Karim Lekadir, Sulaiman Vesal, Nishant RaviKumar, et al. Cardiac segmentation on late gadolinium enhancement mri: A benchmark study from multi-sequence cardiac mr segmentation challenge. *arXiv preprint arXiv:2006.12434*, 2020.