

DeepReg: a deep learning toolkit for medical image registration

Yunguan Fu^{1, 2, 3}, Nina Montaña Brown^{1, 2}, Shaheer U. Saeed^{1, 2}, Adrià Casamitjana², Zachary M. C. Baum^{1, 2}, Rémi Delaunay^{1, 4}, Qianye Yang^{1, 2}, Alexander Grimwood^{1, 2}, Zhe Min¹, Stefano B. Blumberg², Juan Eugenio Iglesias^{2, 5, 6}, Dean C. Barratt^{1, 2}, Ester Bonmati^{1, 2}, Daniel C. Alexander², Matthew J. Clarkson^{1, 2}, Tom Vercauteren⁴, and Yipeng Hu^{1, 2}

1 Wellcome/EPSCRC Centre for Surgical and Interventional Sciences, University College London, London, UK **2** Centre for Medical Image Computing, University College London, London, UK **3** InstaDeep, London, UK **4** Department of Surgical & Interventional Engineering, King's College London, London, UK **5** Martinos Center for Biomedical Imaging, Massachusetts General Hospital and Harvard Medical School, Boston, USA **6** Computer Science and Artificial Intelligence Laboratory, Massachusetts Institute of Technology, Boston, USA

DOI: [10.21105/joss.02705](https://doi.org/10.21105/joss.02705)

Software

- [Review](#) ↗
- [Repository](#) ↗
- [Archive](#) ↗

Editor: [Kevin M. Moerman](#) ↗

Reviewers:

- [@ethanwharris](#)
- [@lbrea](#)
- [@zhangfanmark](#)

Submitted: 01 September 2020

Published: 04 November 2020

License

Authors of papers retain copyright and release the work under a Creative Commons Attribution 4.0 International License ([CC BY 4.0](#)).

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 (Hill et al., 2001), 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 (Fu et al., 2020; Haskins et al., 2020). In addition, its fast inference can substantially accelerate registration execution for time-critical tasks.

DeepReg is a Python package using TensorFlow (Abadi et al., 2015) 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 (Montana Brown et al., 2020), while a recently published research work investigated temporal changes in prostate cancer imaging, by using a longitudinal registration adapted from the *DeepReg* code (Yang et al., 2020).

Statement of need

Currently, popular packages focusing on deep learning methods for medical imaging, such as NiftyNet (Gibson et al., 2018) 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 (Balakrishnan et al., 2019), or focus on classical methods, such as NiftiReg (Modat et al., 2010), SimpleElastix (Marstal et al., 2016) and AirLab (Sandkühler et al., 2018). Therefore an open-sourced project focusing on image registration with deep learning is much needed for general research and education purposes.

Implementation

DeepReg implements a framework for unsupervised learning (Balakrishnan et al., 2019; Vos et al., 2019), weakly-supervised learning (Hu, Modat, Gibson, Li, et al., 2018; Hu, Modat, Gibson, Ghavami, et al., 2018) and their combinations and variants, e.g. (Hu et al., 2019). Many options are included for major components of these approaches, such as different image- and label dissimilarity functions, transformation models (Ashburner, 2007; Hill et al., 2001; Vercauteren et al., 2009), deformation regularisation (Rueckert et al., 1999) and different neural network architectures (He et al., 2016; Hu, Modat, Gibson, Li, et al., 2018; Simonyan & Zisserman, 2014). 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 (Hu, Modat, Gibson, Li, et al., 2018; Yang et al., 2020). 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 (Dalca et al., 2019; Luo & Zhuang, 2020; Siebert & Heinrich, 2020).

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.

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 (Hering et al., 2020), 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 (Hu, Modat, Gibson, Li, et al., 2018). Another DeepReg Demo illustrates MR-to-ultrasound image registration is to track tissue deformation and brain tumour resection during neurosurgery (Xiao et al., 2017).

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 (Simpson et al., 2019), fundamental to population studies. Two other applications align unpaired inter-subject CT images for lung (Hering et al., 2020) and abdominal organs (Dalca et al., 2020). Additionally, the support for cross-validation in DeepReg has been included in a demo, which registers 3D ultrasound images from different prostate cancer patients.

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 (Zhuang et al., 2020), 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 (Yang et al., 2020). 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.

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.

Acknowledgements

This work is supported by the Wellcome/EPSRC Centre for Interventional and Surgical Sciences (203145Z/16/Z). Support was also from the Engineering and Physical Sciences Research Council (EPSRC) (EP/M020533/1, NS/A000049/1), National Institute for Health Research University College London Hospitals Biomedical Research Centre and Wellcome Trust (203148/Z/16/Z). TV is supported by a Medtronic / Royal Academy of Engineering Research Chair (RCSRF1819\7\34). NMB, ZB, RD are also supported by the EPSRC CDT i4health (EP/S021930/1). ZB is supported by the Natural Sciences and Engineering Research Council of Canada Postgraduate Scholarships-Doctoral Program and the University College London Overseas and Graduate Research Scholarships.

References

- Abadi, M., Agarwal, A., Barham, P., Brevdo, E., Chen, Z., Citro, C., Corrado, G. S., Davis, A., Dean, J., Devin, M., Ghemawat, S., Goodfellow, I., Harp, A., Irving, G., Isard, M., Jia, Y., Jozefowicz, R., Kaiser, L., Kudlur, M., ... Zheng, X. (2015). *TensorFlow: Large-scale machine learning on heterogeneous systems*. <https://www.tensorflow.org/>
- Ashburner, J. (2007). A fast diffeomorphic image registration algorithm. *Neuroimage*, 38(1), 95–113. <https://doi.org/10.1016/j.neuroimage.2007.07.007>
- Balakrishnan, G., Zhao, A., Sabuncu, M. R., Guttag, J., & Dalca, A. V. (2019). VoxelMorph: A learning framework for deformable medical image registration. *IEEE Transactions on Medical Imaging*, 38(8), 1788–1800. <https://doi.org/10.1109/TMI.2019.2897538>
- Dalca, A., Hu, Y., Vercauteren, T., Heinrich, M., Hansen, L., Modat, M., Vos, B. de, Xiao, Y., Rivaz, H., Chabanas, M., Reinertsen, I., Landman, B., Cardoso, J., Ginneken, B. van, Hering, A., & Murphy, K. (2020). *Learn2Reg - the challenge*. Zenodo. <https://doi.org/10.5281/zenodo.3715652>

- Dalca, A., Rakic, M., Guttag, J., & Sabuncu, M. (2019). Learning conditional deformable templates with convolutional networks. *Advances in Neural Information Processing Systems*, 806–818.
- Fu, Y., Lei, Y., Wang, T., Curran, W. J., Liu, T., & Yang, X. (2020). Deep learning in medical image registration: A review. *Physics in Medicine & Biology*. <https://doi.org/10.1088/1361-6560/ab843e>
- Gibson, E., Li, W., Sudre, C., Fidon, L., Shakir, D. I., Wang, G., Eaton-Rosen, Z., Gray, R., Doel, T., Hu, Y., & others. (2018). NiftyNet: A deep-learning platform for medical imaging. *Computer Methods and Programs in Biomedicine*, 158, 113–122. <https://doi.org/10.1016/j.cmpb.2018.01.025>
- Haskins, G., Kruger, U., & Yan, P. (2020). Deep learning in medical image registration: A survey. *Machine Vision and Applications*, 31(1), 8. <https://doi.org/10.1007/s00138-020-01066-5>
- He, K., Zhang, X., Ren, S., & Sun, J. (2016). Deep residual learning for image recognition. *Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition*, 770–778. <https://doi.org/10.1109/CVPR.2016.90>
- Hering, A., Murphy, K., & Ginneken, B. van. (2020). *Lean2Reg Challenge: CT Lung Registration - Training Data* [Data set]. Zenodo. <https://doi.org/10.5281/zenodo.3835682>
- Hill, D. L., Batchelor, P. G., Holden, M., & Hawkes, D. J. (2001). Medical image registration. *Physics in Medicine & Biology*, 46(3), R1. <https://doi.org/10.1088/0031-9155/46/3/201>
- Hu, Y., Gibson, E., Barratt, D. C., Emberton, M., Noble, J. A., & Vercauteren, T. (2019). Conditional segmentation in lieu of image registration. *International Conference on Medical Image Computing and Computer-Assisted Intervention*, 401–409. https://doi.org/10.1007/978-3-030-32245-8_45
- Hu, Y., Modat, M., Gibson, E., Ghavami, N., Bonmati, E., Moore, C. M., Emberton, M., Noble, J. A., Barratt, D. C., & Vercauteren, T. (2018). Label-driven weakly-supervised learning for multimodal deformable image registration. *2018 IEEE 15th International Symposium on Biomedical Imaging (ISBI 2018)*, 1070–1074. <https://doi.org/10.1109/ISBI.2018.8363756>
- Hu, Y., Modat, M., Gibson, E., Li, W., Ghavami, N., Bonmati, E., Wang, G., Bandula, S., Moore, C. M., Emberton, M., & others. (2018). Weakly-supervised convolutional neural networks for multimodal image registration. *Medical Image Analysis*, 49, 1–13. <https://doi.org/10.1016/j.media.2018.07.002>
- Luo, X., & Zhuang, X. (2020). MvMM-regnet: A new image registration framework based on multivariate mixture model and neural network estimation. *arXiv Preprint arXiv:2006.15573*. https://doi.org/10.1007/978-3-030-59716-0_15
- Marstal, K., Berendsen, F., Staring, M., & Klein, S. (2016). *SimpleElastix: A user-friendly, multi-lingual library for medical image registration*. 134–142. <https://doi.org/10.1109/CVPRW.2016.78>
- Modat, M., Ridgway, G. R., Taylor, Z. A., Lehmann, M., Barnes, J., Hawkes, D. J., Fox, N. C., & Ourselin, S. (2010). Fast free-form deformation using graphics processing units. *Computer Methods and Programs in Biomedicine*, 98(3), 278–284. <https://doi.org/10.1016/j.cmpb.2009.09.002>
- Montana Brown, N., Fu, Y., Saeed, S. U., Casamitjana, A., Baum, Z. M. C., Delaunay, R., Yang, Q., Grimwood, A., Min, Z., Bonmati, E., Vercauteren, T., Clarkson, M. J., & Hu, Y. (2020). *Introduction to medical image registration with deepreg, between old and new*. https://github.com/DeepRegNet/DeepReg/blob/main/docs/Intro_to_Medical_Image_Registration.ipynb

- Rueckert, D., Sonoda, L. I., Hayes, C., Hill, D. L., Leach, M. O., & Hawkes, D. J. (1999). Nonrigid registration using free-form deformations: Application to breast mr images. *IEEE Transactions on Medical Imaging*, 18(8), 712–721. <https://doi.org/10.1109/42.796284>
- Sandkühler, R., Jud, C., Andermatt, S., & Cattin, P. C. (2018). AirLab: Autograd image registration laboratory. *arXiv Preprint arXiv:1806.09907*.
- Siebert, H., & Heinrich, M. P. (2020). Deep groupwise registration of mri using deforming autoencoders. In *Bildverarbeitung für die medizin 2020* (pp. 236–241). Springer. https://doi.org/10.1007/978-3-658-29267-6_53
- Simonyan, K., & Zisserman, A. (2014). Very deep convolutional networks for large-scale image recognition. *arXiv Preprint arXiv:1409.1556*.
- Simpson, A. L., Antonelli, M., Bakas, S., Bilello, M., Farahani, K., Van Ginneken, B., Kopp-Schneider, A., Landman, B. A., Litjens, G., Menze, B., & others. (2019). A large annotated medical image dataset for the development and evaluation of segmentation algorithms. *arXiv Preprint arXiv:1902.09063*.
- Vercauteren, T., Pennec, X., Perchant, A., & Ayache, N. (2009). Diffeomorphic demons: Efficient non-parametric image registration. *NeuroImage*, 45(1), S61–S72. <https://doi.org/10.1016/j.neuroimage.2008.10.040>
- Vos, B. D. de, Berendsen, F. F., Viergever, M. A., Sokooti, H., Staring, M., & Išgum, I. (2019). A deep learning framework for unsupervised affine and deformable image registration. *Medical Image Analysis*, 52, 128–143. <https://doi.org/10.1016/j.media.2018.11.010>
- Xiao, Y., Fortin, M., Unsgård, G., Rivaz, H., & Reinertsen, I. (2017). 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. <https://doi.org/10.1002/mp.12268>
- Yang, Q., Fu, Y., Giganti, F., Ghavami, N., Chen, Q., Noble, J. A., Vercauteren, T., Barratt, D., & Hu, Y. (2020). *Longitudinal image registration with temporal-order and subject-specificity discrimination*. https://doi.org/10.1007/978-3-030-59716-0_24
- Zhuang, X., Xu, J., Luo, X., Chen, C., Ouyang, C., Rueckert, D., Campello, V. M., Lekadir, K., Vesal, S., RaviKumar, N., & others. (2020). Cardiac segmentation on late gadolinium enhancement mri: A benchmark study from multi-sequence cardiac mr segmentation challenge. *arXiv Preprint arXiv:2006.12434*.