

# CLAIRE: Constrained Large Deformation Diffeomorphic Image Registration on Parallel Computing Architectures

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DOI: [10.21105/joss.03038](https://doi.org/10.21105/joss.03038)

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Submitted: 22 January 2021

Published: 30 May 2021

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## Summary

CLAIRE (Mang & Biros, 2019) is a computational framework for Constrained Large deformation diffeomorphic Image REgistration (Mang et al., 2019). It supports highly-optimized, parallel computational kernels for (multi-node) CPU (Gholami et al., 2017; Mang et al., 2019; Mang & Biros, 2016) and (multi-node multi-)GPU architectures (Brunn et al., 2020, 2021). CLAIRE uses MPI for distributed-memory parallelism and can be scaled up to thousands of cores (Mang et al., 2019; Mang & Biros, 2016) and GPU devices (Brunn et al., 2020). The multi-GPU implementation uses device direct communication. The computational kernels are interpolation for semi-Lagrangian time integration, and a mixture of high-order finite difference operators and Fast-Fourier-Transforms (FFTs) for differentiation. CLAIRE uses a Newton–Krylov solver for numerical optimization (Mang & Biros, 2015, 2017). It features various schemes for regularization of the control problem (Mang & Biros, 2016) and different similarity measures. CLAIRE implements different preconditioners for the reduced space Hessian (Brunn et al., 2020; Mang et al., 2019) to optimize computational throughput and enable fast convergence. It uses PETSc (Balay et al., n.d.) for scalable and efficient linear algebra operations and solvers and TAO (Balay et al., n.d.; Munson et al., 2015) for numerical optimization. CLAIRE can be downloaded at <https://github.com/andreamang/claire>.

## Statement of Need

Image registration is required whenever images are taken at different points in time, from different viewpoints, and/or using different imaging modalities and these images need to be compared, combined, or integrated (Fischer & Modersitzki, 2008; Modersitzki, 2004, 2009; Sotiras et al., 2013). Image registration is an inverse problem. The inputs to this inverse problem are two (or more) images  $m_0(x)$  (the template image) and  $m_1(x)$  (the reference image) of the same object. The task of image registration is to find a plausible map  $y(x)$  that establishes spatial correspondences between the reference and template image, i.e.,  $m_0(x) \approx m_1(y(x))$ . In CLAIRE the set of admissible spatial transformations  $y$  is limited to diffeomorphisms, i.e., maps  $y$  that are continuous, one-to-one, and have a smooth inverse. CLAIRE is related to a prominent class of formulations for these types of problems referred to as large-deformation diffeomorphic metric mapping (Beg et al., 2005; Trounev, 1998; Younes, 2010).

Diffeomorphic image registration is an indispensable tool in medical image analysis (Sotiras et al., 2013). Computing diffeomorphisms that map one image to another is expensive. Deformable image registration is an infinite-dimensional problem that upon discretization leads to

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nonlinear optimality systems with millions or even billions of unknowns. For example, registering two typical medical imaging datasets of size  $256^3$  necessitates solving for about 50 million unknowns (in our formulation). Additional complications are the ill-posedness and non-linearity of this inverse problem (Fischer & Modersitzki, 2008). Consequently, image registration can take several minutes on multi-core high-end CPUs. Many of the available methods reduce the number of unknowns by using coarser resolutions either through parameterization or by solving the problem on coarser grids; they use simplified algorithms and deliver subpar registration quality. In the age of big data, clinical population studies that require thousands of registrations are increasingly common, and execution times of individual registrations become more critical. We provide technology that allows solving registration problems for clinical datasets in seconds. In addition, we have made available to the public a software that works on multi-node, multi-GPU architectures (Brunn et al., 2020, 2021) that allows the registration of large-scale microscopic imaging data such as CLARITY imaging (Kutten et al., 2017; Tomer et al., 2014).

## Highlights

CLAIRE can be used to register images of  $2048^3$  (25 B unknowns) on 64 nodes with 256 GPUs on TACC's Longhorn system (Brunn et al., 2020). CLAIRE has been used for the registration of high resolution CLARITY imaging data (Brunn et al., 2020). The GPU version of CLAIRE can solve clinically relevant problems (50 M unknowns) in approximately 5 seconds on a single NVIDIA Tesla V100 (Brunn et al., 2020). CLAIRE has also been applied to hundreds of images in brain tumor imaging studies (Bakas et al., 2018; Mang et al., 2017; Scheufele et al., 2021), and has been integrated with models for biophysics inversion (Mang et al., 2018, 2020; Scheufele et al., 2019, 2021; Scheufele, Subramanian, Mang, et al., 2020; Subramanian et al., 2020) and Alzheimer's disease progression (Scheufele, Subramanian, & Biros, 2020). CLAIRE uses highly optimized computational kernels and effective, state-of-the-art algorithms for time integration and numerical optimization. Our most recent version of CLAIRE features a Python interface to assist users in their applications.

We provide a detailed documentation on how to execute, compile, and install CLAIRE on various systems at our deployment page <https://andreamang.github.io/claire>.

## Mathematics

CLAIRE uses an optimal control formulation. The diffeomorphism  $y(x)$  is parameterized using a smooth, stationary velocity field  $v(x)$ . Given the template image  $m_0(x)$  and the reference image  $m_1(x)$ , this velocity is found by solving the partial-differential equation constrained optimization problem of the form

$$\text{minimize}_{v,m} \text{dist}(m(x, t = 1), m_1) + \alpha \text{reg}(v)$$

subject to

$$\begin{aligned} \partial_t m(x, t) + v(x) \cdot \nabla m(x, t) &= 0 \\ m(x, t = 0) &= m_0(x) \end{aligned}$$

The first term in the objective functional measures the proximity of the deformed template image  $m(x, t = 1)$  and the reference image  $m_1(x)$ . The default option available in CLAIRE is an  $L^2$ -distance. The second term controls the regularity of  $v$ . CLAIRE features different Sobolev norms. The default option is an  $H^1$ -seminorm. The constraint models the deformation the template image (i.e., the transport of the intensities of  $m_0(x)$ ). CLAIRE also features additional hard constraints for controlling the divergence of  $v(x)$  (Mang & Biros, 2016). For

optimization, we use the method of Lagrange multipliers and solve the associated Karush–Kuhn–Tucker optimality system using a Newton–Krylov reduced space method (Mang & Biros, 2015, 2015).

## Acknowledgements

This work was partly supported by the National Science Foundation (DMS-1854853, DMS-2009923, DMS-2012825, CCF-1817048, CCF-1725743), the NVIDIA Corporation (NVIDIA GPU Grant Program), the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) under Germany's Excellence Strategy-EXC 2075-390740016, by the U.S. Department of Energy, Office of Science, Office of Advanced Scientific Computing Research, Applied Mathematics program under Award Number DE-SC0019393; by the U.S. Air Force Office of Scientific Research award FA9550-17-1-0190; by the Portugal Foundation for Science and Technology and the UT Austin-Portugal program, and by NIH award 5R01NS042645-11A1. Any opinions, findings, and conclusions or recommendations expressed herein are those of the authors and do not necessarily reflect the views of the DFG, AFOSR, DOE, NIH, and NSF. Computing time on the Texas Advanced Computing Centers' (TACC) systems was provided by an allocation from TACC and the NSF. This work was completed in part with resources provided by the Research Computing Data Core at the University of Houston.

## References

- Bakas, S., Reyes, M., Jakab, A., Bauer, S., Rempfler, M., & others. (2018). Identifying the best machine learning algorithms for brain tumor segmentation, progression assessment, and overall survival prediction in the BRATS challenge. *arXiv, 1811.02629*.
- Balay, S., Abhyankar, S., Adams, M. F., Brown, J., Brune, P., Buschelman, K., Dalcin, L., Dener, A., Eijkhout, V., Gropp, W. D., Karpeyev, D., Kaushik, D., Knepley, M. G., May, D. A., McInnes, L. C., Mills, R. T., Munson, T., Rupp, K., Sanan, P., ... Zhang, H. (n.d.). *PETSc and TAO webpage (PETSc version 3.12.4)*. Retrieved 2020, from <https://www.mcs.anl.gov/petsc>
- Beg, M. F., Miller, M. I., Trouvé, A., & Younes, L. (2005). Computing large deformation metric mappings via geodesic flows of diffeomorphisms. *International Journal of Computer Vision, 61*(2), 139–157. <https://doi.org/10.1023/B:VISI.0000043755.93987.a>
- Brunn, M., Himthani, N., Biros, G., Mehl, M., & Mang, A. (2020). Multi-node multi-GPU diffeomorphic image registration for large-scale imaging problems. *Proc ACM/IEEE Conference on Supercomputing*, 1–7. <https://doi.org/10.1109/SC41405.2020.00042>
- Brunn, M., Himthani, N., Biros, G., Mehl, M., & Mang, A. (2021). Fast GPU 3D diffeomorphic image registration. *Journal of Parallel and Distributed Computing, 149*, 149–162. <https://doi.org/10.1016/j.jpdc.2020.11.006>
- Fischer, B., & Modersitzki, J. (2008). Ill-posed medicine – an introduction to image registration. *Inverse Problems, 24*(3), 1–16. <https://doi.org/10.1088/0266-5611/24/3/034008>
- Gholami, A., Mang, A., Scheufele, K., Davatzikos, C., Mehl, M., & Biros, G. (2017). A framework for scalable biophysics-based image analysis. *Proc ACM/IEEE Conference on Supercomputing*, 1–13. <https://doi.org/10.1145/3126908.3126930>
- Kutten, K. S., Charon, N., Miller, M. I., Ratnanather, J. T., Deisseroth, K., Ye, L., & Vogelstein, J. T. (2017). A large deformation diffeomorphic approach to registration of CLARITY images via mutual information. *Proc Medical Image Computing and Computer-Assisted Intervention, LNCS 10433*, 275–282. [https://doi.org/10.1007/978-3-319-66182-7\\_32](https://doi.org/10.1007/978-3-319-66182-7_32)

- Mang, A., Bakas, S., Subramanian, S., Davatzikos, C., & Biros, G. (2020). Integrated biophysical modeling and image analysis: Application to neuro-oncology. *Annual Review of Biomedical Engineering*, 22. <https://doi.org/10.1146/annurev-bioeng-062117-121105>
- Mang, A., & Biros, G. (2015). An inexact Newton–Krylov algorithm for constrained diffeomorphic image registration. *SIAM Journal on Imaging Sciences*, 8(2), 1030–1069. <https://doi.org/10.1137/140984002>
- Mang, A., & Biros, G. (2016). Constrained  $H^1$ -regularization schemes for diffeomorphic image registration. *SIAM Journal on Imaging Sciences*, 9(3), 1154–1194. <https://doi.org/10.1137/15m1010919>
- Mang, A., & Biros, G. (2017). A Semi-Lagrangian two-level preconditioned Newton–Krylov solver for constrained diffeomorphic image registration. *SIAM Journal on Scientific Computing*, 39(6), B1064–B1101. <https://doi.org/10.1137/16m1070475>
- Mang, A., & Biros, G. (2019). *Constrained large deformation diffeomorphic image registration (CLAIRE)*. <https://andreamang.github.io/claire>
- Mang, A., Gholami, A., Davatzikos, C., & Biros, G. (2018). PDE-constrained optimization in medical image analysis. *Optimization and Engineering*, 19(3), 765–812. <https://doi.org/10.1007/s11081-018-9390-9>
- Mang, A., Gholami, A., Davatzikos, C., & Biros, G. (2019). CLAIRE: A distributed-memory solver for constrained large deformation diffeomorphic image registration. *SIAM Journal on Scientific Computing*, 41(5), C548–C584. <https://doi.org/10.1137/18M1207818>
- Mang, A., Tharakan, S., Gholami, A., Nimthani, N., Subramanian, S., Levitt, J., Azmat, M., Scheufele, K., Mehl, M., Davatzikos, C., Barth, B., & Biros, G. (2017). SIBIA-GIS: Scalable biophysics-based image analysis for glioma segmentation. *Proc BraTS 2017 Workshop*, 197–204.
- Modersitzki, J. (2004). *Numerical methods for image registration*. Oxford University Press. <https://doi.org/10.1093/acprof:oso/9780198528418.001.0001>
- Modersitzki, J. (2009). *FAIR: Flexible algorithms for image registration*. SIAM. <https://doi.org/10.1137/1.9780898718843>
- Munson, T., Sarich, J., Wild, S., Benson, S., & McInnes, L. C. (2015). *TAO 3.6 users manual*. Argonne National Laboratory, Mathematics; Computer Science Division.
- Scheufele, K., Mang, A., Gholami, A., Davatzikos, C., Biros, G., & Mehl, M. (2019). Coupling brain-tumor biophysical models and diffeomorphic image registration. *Computer Methods in Applied Mechanics and Engineering*, 237, 533–567. <https://doi.org/10.1016/j.cma.2018.12.008>
- Scheufele, K., Subramanian, S., & Biros, G. (2020). Calibration of biophysical models for tau-protein spreading in Alzheimer’s disease for PET-MRI. *arXiv, 2007.01236*, 1–11.
- Scheufele, K., Subramanian, S., & Biros, G. (2021). Fully automatic calibration of tumor-growth models using a single mpMRI scan. *IEEE Transactions on Medical Imaging*, 40(1), 193–204. <https://doi.org/10.1109/TMI.2020.3024264>
- Scheufele, K., Subramanian, S., Mang, A., Biros, G., & Mehl, M. (2020). Image-driven biophysical tumor growth model calibration. *SIAM Journal on Scientific Computing*, 42(3), B549–B580. <https://doi.org/10.1137/19M1275280>
- Sotiras, A., Davatzikos, C., & Paragios, N. (2013). Deformable medical image registration: A survey. *Medical Imaging, IEEE Transactions on*, 32(7), 1153–1190. <https://doi.org/10.1109/TMI.2013.2265603>
- Subramanian, S., Scheufele, K., Himthani, N., & Biros, G. (2020). Multiatlas calibration of biophysical brain tumor growth models with mass effect. *Proc Medical Image Computing*

and Computer Assisted Intervention, LNCS 12262, 551–560. [https://doi.org/10.1007/978-3-030-59713-9\\_53](https://doi.org/10.1007/978-3-030-59713-9_53)

Tomer, R., Ye, L., Hsueh, B., & Deisseroth, K. (2014). Advanced CLARITY for rapid and high-resolution imaging of intact tissues. *Nature Protocols*, 9(7), 1682–1697. <https://doi.org/10.1038/nprot.2014.123>

Trouvé, A. (1998). Diffeomorphism groups and pattern matching in image analysis. *International Journal of Computer Vision*, 28(3), 213–221. <https://doi.org/10.1023/A:1008001603737>

Younes, L. (2010). *Shapes and diffeomorphisms*. Springer-Verlag Berlin Heidelberg. <https://doi.org/10.1007/978-3-642-12055-8>