A Flexible Variational Registration Framework

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Abstract

In this article, we present an implementation of a flexible framework for non-parametric variational image registration, realized as part of ITK's finite difference solver hierarchy.
In a variational registration setting, the transformation is found by minimizing an energy functional that consists of (at least) two terms: a distance measure between fixed and transformed moving image and a smoothness condition for the transformation. The specific choice of these terms depends on the particular application and requires consideration of, for example, image content and imaging modalities. Following this view, the presented framework can be seen as a generalization of the demons algorithm in which two key aspects remain exchangeable: the *force term* (or registration function, according to the distance measure) and the *regularizer* (according to the smoothness condition). Moreover, two *transformation models* are realized: either a dense displacement field or a stationary velocity field to restrain the transformation to the space of diffeomorphisms.
In its current state, the framework includes implementations of forces based on the Sum of Squared Differences (SSD), Normalized Cross Correlation (NCC) and the demons algorithm as well as Gaussian, diffusion and elastic smoothing. However, the implementation of further components is possible and encouraged.

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Contents

Forewords

This paper is meant to complement the article "Estimation of lung motion fields in 4D CT data by variational non-linear intensity-based registration: A comparison and evaluation study" [12], in which the authors present an extensive comparison study of different registration algorithms for the estimation of respiratory motion on the base of 4D CT data. It presents the source code of the applied registration approaches and gives details about the implementation. The final idea is to allow the reader to reproduce the results presented in [12] by using the provided code and the publicly available image and evaluation data of the CREATIS [11] and DIR-lab 4D CT data bases [3].
Moreover, the framework implements the principal algorithm presented in [9], which was ranked with an initial forth place at the EMPIRE10 registration challenge [7].[1] It was further employed in [4].
This paper provides only basic information about the underlying theory of the registration framework; for further information on this subject, the reader is referred to the underlying and above-mentioned articles [12, 9] and references therein.

1 Introduction

Image registration is a crucial aspect of many applications in Medical Imaging. During the past years, a wide variety of approaches has been proposed and successfully applied for diverse registration tasks.
A very prominent example is the demons algorithm, of which an open source implementation is available

[1] At the time of writing, [9] holds rank ten at the EMPIRE10 challenge.

in the Insight Segmentation and Registration Toolkit. The algorithm consists of two main parts: the calculation of demon forces and a Gaussian smoothing of the accumulated displacement field. However, many applications demand a specific adaption of these parts to a particular task.
A variational interpretation of the registration problem allows to generalize the demons algorithm in order to adapt it to specific tasks and applications. In this way, force calculation and regularization remain exchangeable.
In this work, we present present an implementation of a flexible framework for variational image registration. Within this framework, force term and regularizer can be easily exchanged. As examples, we implemented Sum of Squared Differences-, Normalized Cross Correlation-, and demon-based forces as well as diffusion, elastic and Gaussian regularization terms. Other terms can be integrated easily.

2 Methods

2.1 Variational formulation of the image registration problem

Without going into mathematical detail (which can be found, for example, in [5]), the goal of image registration can be formulated as finding a transformation $\varphi(\boldsymbol{x})$ that minimizes the distance $\mathcal{D}$ between a fixed image $F(\boldsymbol{x})$ and a transformed moving image $M \circ \varphi(\boldsymbol{x})$ with respect to an intended smoothness $\mathcal{S}$ of the transformation:

$$\mathcal{J}[\varphi] := \mathcal{D}[F,M;\varphi] \; + \; \mathcal{S}[\varphi] = \min! \tag{1}$$

The specific choice of the terms $\mathcal{D}$ and $\mathcal{S}$ strongly depends on the particular application.
The first consideration for choosing the distance measure is usually whether the images are mono- or multi-modal. Common formulations for mono-modal registration include the *Sum of Squared Differences* (SSD), whereas *Normalized Cross Correlation* (NCC), *Normalized Mutual Information* (NMI) or the *Normalized Gradient Field* (NGF) are also used for multi-modal problems.
Popular choices for the smoothness condition include, for example, diffusion and elastic regularization.
In the basic approach, the transformation is given by a dense displacement field $\boldsymbol{u}$, with $\varphi(\boldsymbol{x}) := \boldsymbol{x} + \boldsymbol{u}(\boldsymbol{x})$. In this case, the Euler-Lagrange equation associated with the minimization of $\mathcal{J}[\varphi]$ leads to the necessary condition

$$\mathcal{A}[\boldsymbol{u}](\boldsymbol{x}) - f(\boldsymbol{u}(\boldsymbol{x})) = 0\,.$$

Here, $\boldsymbol{f}$ denotes a force field that is related to the Gateaux-derivative of the distance measure $\mathcal{D}[F,M;\varphi]$ and $\mathcal{A}$ is a linear partial differential operator, which can be deduced from the Gateaux-derivative of $\mathcal{S}[\varphi]$ (cf. [5]).
To solve (1), the semi-implicit scheme

$$\boldsymbol{u}^{(k+1)} = (Id - \tau\mathcal{A})^{-1}\left(\boldsymbol{u}^{(k)} + \tau\boldsymbol{f}(\boldsymbol{u}^{(k)})\right) \tag{2}$$

is employed, where Id denotes the identity mapping and τ is the step size. The resulting registration scheme is summarized in Algorithm 1.

2.2 Diffeomorphic and symmetric diffeomorphic registration

Following the approach of Arsigny [1], diffeomorphisms are defined as solutions of the stationary flow equation at $t = 1$

$$\frac{\partial}{\partial t}\phi(\boldsymbol{x},t) = \boldsymbol{v}(\phi(\boldsymbol{x},t)),\ \phi(\boldsymbol{x},0) = \boldsymbol{x}\ , \tag{3}$$

Algorithm 1 Variational registration

Set $\boldsymbol{u}^{(0)} = 0$ or to an initial field and $k = 0$
repeat
  Compute the update field $\boldsymbol{p}^{(k)} = \tau \boldsymbol{f}(\boldsymbol{u}^{(k)})$
  Let $\boldsymbol{u}^{(k)} \leftarrow \boldsymbol{u}^{(k)} + \boldsymbol{p}^{(k)}$
  Regularize the displacement field using $\boldsymbol{u}^{(k+1)} = (Id - \tau\mathcal{A})^{-1}\,\boldsymbol{u}^{(k)}$
  Let $k \leftarrow k+1$
until $k \geq K_{max}$ or another stop criterion is fulfilled

Algorithm 2 Diffeomorphic variational registration

Set $\boldsymbol{v}^{(0)} = 0$ or to an initial field, $\boldsymbol{u}^{(0)} = \exp(\boldsymbol{v}^{(0)}) - \boldsymbol{x}$ and $k = 0$
repeat
  Compute the update step $\boldsymbol{p}^{(k)} = \tau \boldsymbol{f}(\boldsymbol{u}^{(k)})$
  Let $\boldsymbol{v}^{(k)} \leftarrow \boldsymbol{v}^{(k)} + \boldsymbol{p}^{(k)}$
  Regularize the velocity field using $\boldsymbol{v}^{(k+1)} = (Id - \tau\mathcal{A})^{-1}\,\boldsymbol{v}^{(k)}$
  Calculate the corresponding displacement field $\boldsymbol{u}^{(k+1)} = \exp(\boldsymbol{v}^{(k+1)}) - \boldsymbol{x}$
  Let $k \leftarrow k+1$
until $k \geq K_{max}$ or another stop criterion is fulfilled

where $\boldsymbol{v}(\boldsymbol{x})$ is a stationary vector field (the velocity field of the transformation). The solution of (3) is given by the group exponential map $\varphi(\boldsymbol{x}) = \phi(\boldsymbol{x}, 1) = \exp(\boldsymbol{v}(\boldsymbol{x}))$. Exploiting this approach, the update scheme for diffeomorphic registration is defined on the basis of the velocity fields of the transformation,

$$\boldsymbol{v}^{(k+1)} = (Id - \tau\mathcal{A})^{-1}\left(\boldsymbol{v}^{(k)} + \tau \boldsymbol{f}(\boldsymbol{v}^{(k)})\right) , \tag{4}$$

with the corresponding displacement field given by

$$\boldsymbol{u}^{(k+1)} = \exp(\boldsymbol{v}^{(k+1)}) - \boldsymbol{x} .$$

The resulting diffeomorphic registration scheme can be summarized as listed in Algorithm 2.
Finally, the immediate availability of the inverse transformation $\varphi^{-1}(\boldsymbol{x}) = \exp(-\boldsymbol{v}(\boldsymbol{x}))$ enables an efficient implementation of a symmetric variant of the algorithm with

$$\mathcal{D}^{Sym}[F, M; \varphi] = \frac{1}{2}\left(\mathcal{D}[F, M; \varphi] + \mathcal{D}[M, F; \varphi^{-1}]\right) .$$

When this term is applied, the result is independent of the choice of the fixed image. This leads to the symmetric diffeomorphic registration variant summarized in algorithm 3.

2.3 Force terms

In the following section, the force terms currently implemented in the framework are described. In [12], registration methods were applied for motion estimation in 4D CT data and therefore the focus was on mono-modal distance measures (see the respective literature overview in the article for motivation of the specific choice of the implemented distance measures). The implementation of further force terms like NMI oder NGF is subject of future work.

Algorithm 3 Symmetric diffeomorphic variational registration

Set $\boldsymbol{v}^{(0)} = 0$ or to an initial field, $\boldsymbol{u}^{(0)} = \exp(\boldsymbol{v}^{(0)}) - \boldsymbol{x}$, $\boldsymbol{w}^{(0)} = \exp(-\boldsymbol{v}^{(0)}) - \boldsymbol{x}$ and $k = 0$
repeat
  Compute the update step $\boldsymbol{p}^{(k)} = \tau \boldsymbol{f}(\boldsymbol{u}^{(k)}, \boldsymbol{w}^{(k)})$
  Let $\boldsymbol{v}^{(k)} \leftarrow \boldsymbol{v}^{(k)} + \boldsymbol{p}^{(k)}$
  Regularize the velocity field using $\boldsymbol{v}^{(k+1)} = (Id - \tau\mathcal{A})^{-1}\,\boldsymbol{v}^{(k)}$
  Calculate the corresponding displacement field $\boldsymbol{u}^{(k+1)} = \exp(\boldsymbol{v}^{(k+1)}) - \boldsymbol{x}$
  Calculate the inverse displacement field $\boldsymbol{w}^{(k+1)} = \exp(-\boldsymbol{v}^{(k+1)}) - \boldsymbol{x}$
  Let $k \leftarrow k+1$
until $k \geq K_{max}$ $k \geq K_{max}$ or another stop criterion is fulfilled

SSD forces

A common choice for the distance measure is the *Sum of Squared Differences* (SSD) between fixed image and transformed target image:

$$\mathcal{D}^{SSD}[F,M;\varphi] := \int_{\Omega} \left(F(\boldsymbol{x}) - M\circ\varphi(\boldsymbol{x})\right)^2 \, d\boldsymbol{x} \; .$$

The derivation of $\mathcal{D}^{SSD}$ leads to the force term

$$\boldsymbol{f}^{SSD}(\boldsymbol{u}) := (F - M\circ\varphi)\,\nabla M\circ\varphi \; .$$

Demon forces

In [10], Thirion introduced the *demon-based registration* with some alternative force formulations that play the same role as $\boldsymbol{f}^{SSD}$. Contrary to the SSD-based force,

$$\boldsymbol{f}^{NSSDa}(\boldsymbol{u}) := \frac{F - M\circ\varphi}{\|\nabla M\circ\varphi\|^2 + \alpha\cdot(F - M\circ\varphi)^2}\nabla M\circ\varphi$$

induces relatively stronger forces in regions with low image contrast by utilizing the normalized gradient (NSSD = *Normalized* Sum of Squared Differences). The parameter $\alpha \neq 0$ is used to prevent instability in regions with a contrast close to zero. Analogous to the `itk::DemonsRegistrationFunction`, we use $\alpha = 1/\delta_{\boldsymbol{x}}^2$ with $\delta_{\boldsymbol{x}}^2$ denoting the mean squared spacing of the image.
In $\boldsymbol{f}^{NSSDa}$, the *warped moving image* is used for gradient calculation, which causes an *active force* “pushing” the target image to fit the reference image. However, in

$$\boldsymbol{f}^{NSSDp}(\boldsymbol{u}) := \frac{F - M\circ\varphi}{\|\nabla F\|^2 + \alpha\cdot(F - M\circ\varphi)^2}\nabla F$$

the *fixed image* is used for gradient calculation, leading to a *passive force* “pulling” the target image. This term provides computational advantages because gradients are not calculated in each iteration.
As a combination of these two terms, the symmetric or *dual force term*

$$\boldsymbol{f}^{NSSDd}(\boldsymbol{u}) := \frac{(F - M\circ\varphi)\cdot(\nabla F + \nabla M\circ\varphi)}{\|\nabla F + \nabla M\circ\varphi\|^2 + \alpha\cdot(F - M\circ\varphi)^2}$$

was proposed.
N.B.: Both $\boldsymbol{f}^{NSSDa}$ and $\boldsymbol{f}^{NSSDp}$ are closely related to the second order approximation of the SSD gradient. Still, for the best of our knowledge, the exact energy corresponding to these terms is not known for the particular choice of α (cf. [8]).

NCC forces

Normalized Cross Correlation (NCC) of two images F and M can be understood as

$$NCC[F,M] := \frac{\int_\Omega F(\boldsymbol{x})M(\boldsymbol{x})\,d\boldsymbol{x}}{\int_\Omega F(\boldsymbol{x})^2\,d\boldsymbol{x}\ \int_\Omega M(\boldsymbol{x})^2\,d\boldsymbol{x}}\ ,$$

with the corresponding NCC-based distance measure (i.e., the energy to minimize) given by $1-NCC[F,M]^2$; cf. [6]. For implementation of the distance measure, we followed [2] and defined $\mathcal{D}^{NCC}$ on the discretized image domain $\Omega^\#$:

$$\begin{aligned}\mathcal{D}^{NCC}[F,M;\varphi] &:= 1-\frac{\left[\sum_{\boldsymbol{x}\in\Omega^\#}\left(F(\boldsymbol{x})-\bar{F}(\boldsymbol{x})\right)\left(M\circ\varphi(\boldsymbol{x})-\bar{M}\circ\varphi(\boldsymbol{x})\right)\right]^2}{\sum_{\boldsymbol{x}\in\Omega^\#}\left(F(\boldsymbol{x})-\bar{F}(\boldsymbol{x})\right)^2\sum_{\boldsymbol{x}\in\Omega^\#}\left(M\circ\varphi(\boldsymbol{x})-\bar{M}\circ\varphi(\boldsymbol{x})\right)^2}\\ &=: 1-\frac{A^2}{BC}\ . \end{aligned} \tag{5}$$

The terms $\bar{F}(\boldsymbol{x})$ and $\bar{F}(\boldsymbol{x})$ denote average intensity values, computed over a local neighborhood of $\boldsymbol{x}$ in F and M, respectively. Based on (5), NCC forces finally read as

$$f^{NCC}(\boldsymbol{u}) := -\frac{2A}{BC}\left(\left(F(\boldsymbol{x})-\bar{F}(\boldsymbol{x})\right)-\frac{A}{C}\left(M\circ\varphi(\boldsymbol{x})-\bar{M}\circ\varphi(\boldsymbol{x})\right)\right)\nabla\left(M-\bar{M}\right)\circ\varphi(\boldsymbol{x})\ . \tag{6}$$

2.4 Regularizers

Diffusion regularization

In diffusion regularization, the gradient of the deformation is penalized. The term is given by

$$\mathcal{S}^{\text{diff}}[\boldsymbol{u}] := \frac{1}{2}\int_\Omega\sum_{l=1}^{3}\|\nabla u_l(\boldsymbol{x})\|^2 d\boldsymbol{x}.$$

This leads to the Laplace operator as associated linear differential operator, i.e.

$$\mathcal{A}^{\text{diff}}[\boldsymbol{u}] := \Delta\boldsymbol{u}. \tag{7}$$

The main reason for introducing the diffusion regularizer in image registration is its low computational complexity of $O(N)$ with N being the number of image voxels. This can be achieved using *Additive Operator Splitting* (AOS) [5].

Elastic regularization

The elastic regularizer measures the elastic potential

$$\mathcal{S}^{\text{elastic}}[\boldsymbol{u}] := \mathcal{P}[\boldsymbol{u}] = \int_\Omega\frac{\mu}{4}\sum_{i,k=1}^{d}\left(\partial_{x_i}u_k+\partial_{x_k}u_i\right)^2+\frac{\lambda}{2}\left(\nabla\cdot\boldsymbol{u}\right)^2 d\boldsymbol{x}$$

of the deformation. The associated differential operator is given by the Navier-Lamé operator

$$\mathcal{A}^{\text{elastic}}[\boldsymbol{u}] := \mu\Delta\boldsymbol{u}+(\lambda+\mu)\nabla(\nabla\cdot\boldsymbol{u}) \tag{8}$$

where μ and λ are the Lamé constants that constitute a parameterization of the elastic moduli for the media modeled. By performing regularization in Fourier space, complexity can be reduced to $O(N\log N)$ [5].

Gaussian regularization

In a strict mathematical sense, Gaussian regularization is not an implementation of scheme (2) but writes as

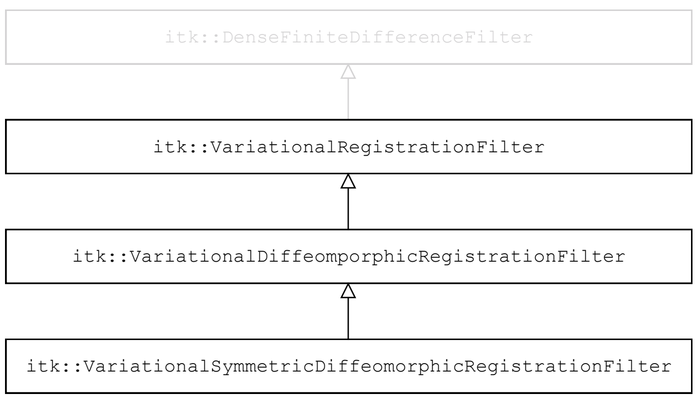
$$\boldsymbol{u}^{(k+1)} = K_\sigma * \left(\boldsymbol{u}^{(k)} + \boldsymbol{f}(\boldsymbol{u}^{(k)})\right) ,$$

where K_σ denotes a Gauss kernel with standard deviation σ. However, it is closely related to the diffusion regularization $\mathcal{S}^{diff}$ and can be seen as an analytical solution of the problem rather than the numerical scheme stated above [5].
In conjunction with demon forces, Gaussian regularization allows to compose the classical demons algorithm with the presented variational registration framework.

3 Implementation details

3.1 Registration filter

The registration filter is implemented as an `itk::DenseFiniteDifferenceImageFilter`. Output and (mandatory) input image is the displacement field of the transformation (the denotation "deformation field" was used in ITK 3.x but then corrected to "displacement field" in ITKv4).



Declaration of the registration filter is done as follows:

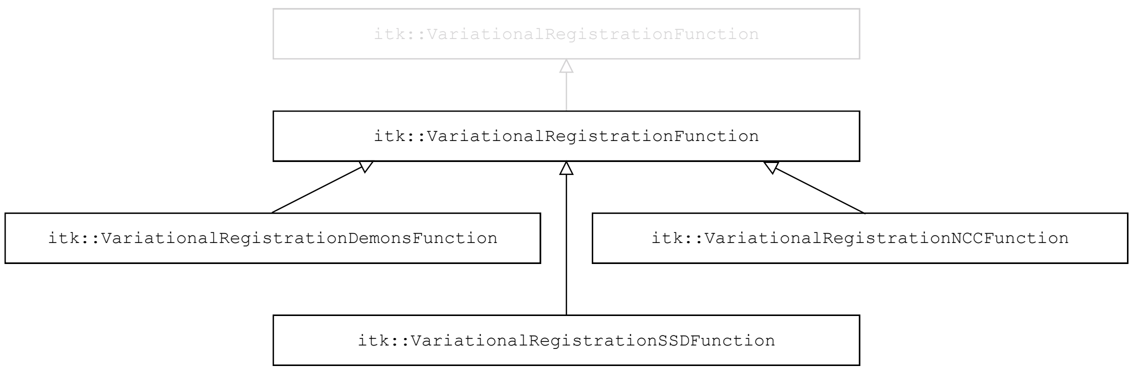
```
typedef VariationalRegistrationFilter<
    FixedImageType,
    MovingImageType,
    DisplacementFieldType > RegistrationFilterType;

RegistrationFilterType::Pointer registrationFilter;

registrationFilter = RegistrationFilterType::New();
```

3.2 Diffeomorphic and symmetric diffeomorphic registration filter

In contrast to the standard registration filter, the diffeomorphic filters take the velocity field as input and output, respectively. The corresponding displacement field is calculated internally from the velocity using the itk::ExponentialDisplacementFieldImageFilter and can be accessed via GetDisplacementField(). This allows to handle both filters consistently in a multi resolution setting.

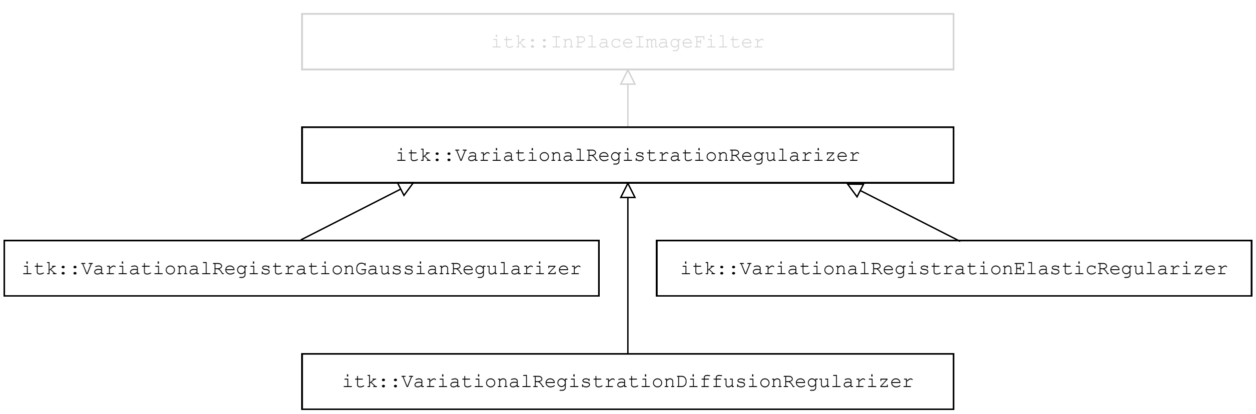
3.3 Force terms

Force terms are realized as implementations of the itk::FiniteDifferenceFunction. They share the common interface itk::VariationalRegistrationFunction.
For all forces, a mask image can be defined using SetMaskImage() in order to execute the registration only in a certain region.



3.4 Regularizers

Regularizers are realized as stand-alone itk::InPlaceImageFilters, which means that they can also be used separately from the framework. They share the common interface itk::VariationalRegistration-Regularizer. The itk::VariationalRegistrationElasticRegularizer performs a Fourier transformation and is therefore only available if ITK is built with USE_FFTWD or USE_FFTWF flag on.



4 User's guide

4.1 Building the framework

The provided variational registration implementation was tested using the Insight Toolkit in a version of 4.4 and CMake 2.8. We make use of classes like `itk::ExponentialDisplacementFieldImageFilter` that are currently in the "Review" directory; therefore, ITK must be built with the ITK_USE_REVIEW flag on. Furthermore, the `itk::VariationalRegistrationElasticRegularizer` uses FFTW (tested with the built-in version 3.2.2). In order to use this class, an installation of the framework must be provided and ITK must be built with the USE_FFTWD and/or USE_FFTWF flag on.

4.2 Class overview

- `itk::VariationalRegistrationFilter<TFixedImage, TMovingImage, TDisplacementField>`: The registration filter.
- `itk::VariationalDiffeomorphicRegistrationFilter<TFixedImage, TMovingImage, TDisplacementField>`: The diffeomorphic registration filter.
- `itk::VariationalSymmetricDiffeomorphicRegistrationFilter<TFixedImage, TMovingImage, TDisplacementField>`: The symmetric diffeomorphic registration filter.
- `itk::VariationalRegistrationMultiResolutionFilter<TFixedImage, TMovingImage, TDisplacementField>`: A filter for performing the registration in a multi resolution setting.
- `itk::VariationalRegistrationFunction<TFixedImage, TMovingImage, TDisplacementField>`: Base class for all registration functions used in the framework.
- `itk::VariationalRegistrationDemonsFunction<TFixedImage, TMovingImage, TDisplacementField>`: Implementation of the demons function/force term, see 2.3.
- `itk::VariationalRegistrationSSDFunction<TFixedImage, TMovingImage, TDisplacementField>`: Implementation of the SSD function/force term, see 2.3.
- `itk::VariationalRegistrationNCCFunction<TFixedImage, TMovingImage, TDisplacementField>`: Implementation of the NCC function/force term, see 2.3.
- `itk::VariationalRegistrationRegularizer<TDisplacementField, TDisplacementField>`: Base class for all regularizers used in the framework.
- `itk::VariationalRegistrationGaussianRegularizer<TDisplacementField, TDisplacementField>`: Implementation of the Gaussian smoothing, see 2.4.
- `itk::VariationalRegistrationDiffusionRegularizer<TDisplacementField, TDisplacementField>`: Implementation of the diffusion smoothing, see 2.4.
- `itk::VariationalRegistrationElasticRegularizer<TDisplacementField, TDisplacementField>`: Implementation of the elastic smoothing, see 2.4.
- `itk::VariationalRegistrationStopCriterion<TRegistrationFilter, TMultiResolutionFilter>`: A stop criterion for the registration implemented as an observer.

- `itk::ContinuousBorderWarpImageFilter<TInputImage,TOutputImage,TDisplacementField>`: An image warping filter that assumes a continuous boundary. This filter can be used separatly from the module.

4.3 Example program

With `itkVariationalRegistration`, an example program is provided for testing the different registration approaches. The simplest execution command is

```
./bin/VariationalRegistration -M Moving.nii.gz -F Fixed.nii.gz -D OutDisplacement.mha
```

The following parameters can be used to specify the algorithm:

- `-F <STRING>`: Filename of the fixed image
- `-M <STRING>`: Filename of the moving image
- `-S <STRING>`: Filename of the mask segmentation for the registration
- `-I <STRING>`: Filename of the initial displacement field
- `-O <STRING>`: Filename of the output displacement field
- `-V <STRING>`: Filename of the output velocity field (for diffeomorphic registration)
- `-W <STRING>`: Filename of the output warped moving image
- `-L <STRING>`: Filename of the log file of the registration
- `-i <UINT>`: Number of iterations
- `-l <UINT>`: Number of multi-resolution levels
- `-t <FLOAT>`: Registration time step
- `-s <UINT>`: Select search space: `0`: Standard (default), `1`: Diffeomorphic, `2`: Sym. diffeomorphic
- `-u <UINT>`: Use image spacing: `0`: false, `1`: true (default)
- `-u <UINT>`: Number of scaling and squaring iterations (for diffeomorphic registration)
- `-r <UINT>`: Select regularizer: `0`: Gaussian smoother (default), `1`: Diffusion, `2`: Elastic
- `-a <FLOAT>`: Alpha for the regularization (only diffusive)
- `-v <FLOAT>`: Variance for the regularization (only gaussian)
- `-m <FLOAT>`: Mu for the regularization (only elastic)
- `-b <FLOAT>`: Lambda for the regularization (only elasic)
- `-f <UINT>`: Select force term: `0`: Demon forces (default), `1`: SSD forces, `2`: NCC forces
- `-q <UINT>`: Neighbourhood size for NCC calculation

- `-d <UINT>`: Select image domain for force calculation: `0`: Active or warped image forces (default), `1`: Passive or fixed image forces, `2`: Dual or symmetric forces
- `-p <UINT>`: Select stop criterion policy
- `-g <FLOAT>`: Set fitted line slope for stop criterion
- `-h <UINT>`: Perform histogram matching: `0`: false (default), `1`: true
- `-x`: Print debug information
- `-3`: Print output field as 3D field in 2D implementation
- `-?`: Print help

5 Conclusion

We have presented an implementation of a variational registration framework for ITK, which can be seen as a more flexible alternative to the demons algorithm. While large parts of the code are based on existing implementations, completely new core functionalities have been added to the framework. For example, to the best of our knowledge, there is currently no implementation of elastic or diffusion regularization available in ITK.

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