Multi-objective optimization for deformable image registration: proof of concept

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ABSTRACT

In this work we develop and study a methodology for deformable image registration that overcomes a drawback of optimization procedures in common deformable image registration approaches: the use of a single combination of different objectives. Because selecting the best combination is well-known to be non-trivial, we use a multi-objective optimization approach that computes and presents multiple outcomes (a so-called Pareto front) at once. The approach is inherently more powerful because not all Pareto-optimal outcomes are necessarily obtainable by running existing approaches multiple times, for different combinations. Furthermore, expert knowledge can be easily incorporated in making the final best-possible decision by simply looking at (a diverse selection of) the outcomes illustrating both the transformed image and the associated deformation vector field. At the basis of the optimization methodology lies an advanced, model-based evolutionary algorithm that aims to exploit features of a problem's structure in a principled manner via probabilistic modeling. Two objectives are defined: 1) maximization of intensity similarity (normalized mutual information) and 2) minimization of energy required to accomplish the transformation (a model based on Hooke's law that incorporates elasticity characteristics associated with different tissue types). A regular grid of points forms the basis of the transformation model. Interpolation extends the correspondence as found for the grid to the rest of the volume. As a proof of concept we performed tests on a 2D axial slice of a CT scan of a breast. Results indicate plausible behavior of the proposed methodology that innovatively combines intensity-based and model-based registration criteria with state-of-the-art adaptive computation techniques for multi-objective optimization in deformable image registration.

Keywords: Multi-objective optimization, evolutionary algorithms, deformable registration

1. INTRODUCTION

Over the past few decades advances in computer science have led to image processing techniques that have proven useful for healthcare.[1] One particular image processing task that can be of great value for healthcare, is deformable image registration. Various deformable image registration techniques have been developed.[2] However, despite significant progress, deformable registration is still not broadly used in clinical practice and challenging problems still remain.[3]

Existing deformable registration techniques compute the outcome of registration based on a single combination of different objectives. Typically, these objectives are related to the image similarity and the smoothness of the transformation. It is, however an unsolved problem how to select the singular optimal combination of objectives beforehand, making clinical implementation of such algorithms difficult. Different combinations lead to different outcomes, which can ultimately only be judged in quality by experts.

In this paper, we propose to take a multi-objective optimization approach to deformable image registration. Such an approach removes the need for a predetermined singular combination of objectives in deformable

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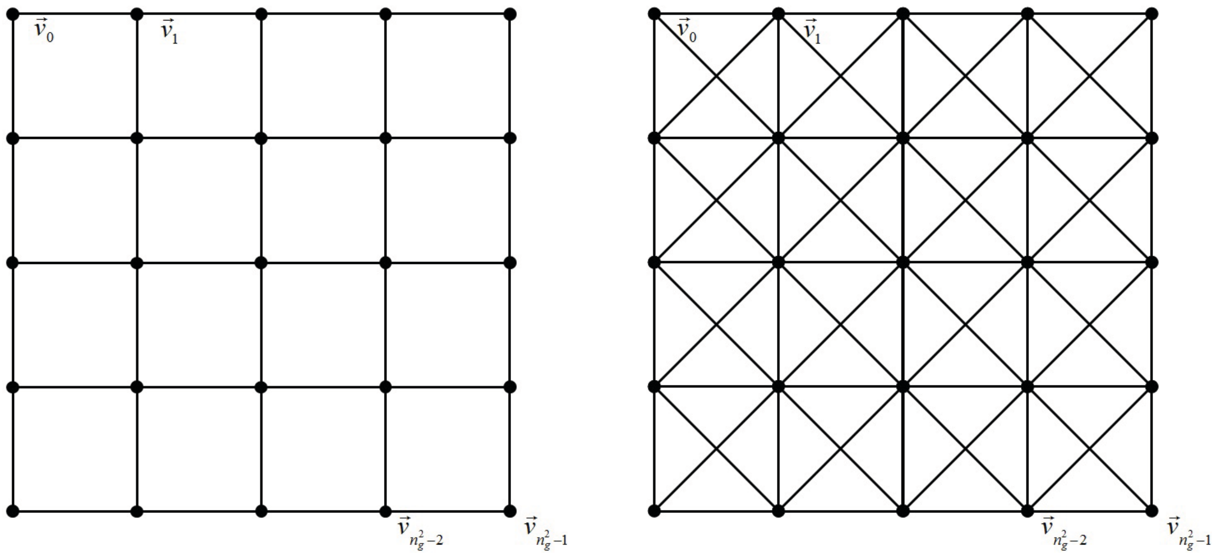

Figure 1. Left: grid of points used as a basis for the transformation model. Right: grid of points with all connections taken into account in the calculation of the required energy to accomplish a transformation.

registration. By computing and presenting multiple outcomes that represent efficient trade-offs between the objectives (a so-called Pareto front) at once, a transparent manner of incorporating expert knowledge is obtained for making the final best-possible decision for the situation at hand.

2. MATERIALS AND METHODS

The general idea of image registration is to find a transformation that transforms a source image to a target image. For the task of image registration two issues are of prime interest: 1) intensity similarity, i.e. the degree of similarity between intensity patterns in the target image and the transformed source image, and 2) transformation effort, i.e. the amount of energy required to accomplish the transformation. In the following we provide rudimentary, but computationally useful definitions for these issues.

2.1 Transformation model

The transformation model, i.e. the representation of possible transformations, is often based on a regular grid of points.[4] Here, we used a square grid of size $n_g \times n_g$, although it should be noted that our overall approach is not restricted to using square grids. The grid overlays the source image in a regular manner, meaning that it corresponds to a subdivision of the source image into $(n_g - 1)(n_g - 1)$ equally-sized axes-parallel rectangles (see Figure 1). The actual transformation then is given by the association of coordinates with each point in the grid. A means of interpolation is required to extend the so-established correspondence between grids to create the transformed source image. To this end, in this paper we use bi-linear interpolation in each rectangle.

2.2 Similarity measure

The preferred transformation is one that maximizes similarity between the target image and the transformed source image. We model similarity in intensity with a measure (to be maximized) that is commonly adopted in registration literature, namely normalized mutual information: $(H(T[s]) + H(t))/H(T[s], t)$, where $H(T[s])$, $H(t)$ and $H(T[s], t)$ denote the entropy of the probability distribution of the grey values in the transformed source image, the entropy of the probability distribution of the grey values in the target image and the entropy of the joint probability distribution of the grey values (i.e. for the registered pairs of pixels) in the transformed source image and the target image, respectively.[5]

2.3 Deformation energy

Ideally, only transformations which are physically realistic for the application in mind should be considered. To associate physical characteristics with transformations, Hooke's law is used.[6] Because we are interested in non-rigid transformations, transformations such as rotations and translations of the entire grid should not correspond to an increase in energy. The required energy is therefore computed on the basis of changes in the lengths of edges in the grid. To ensure that the physical changes we are interested in, i.e. non-rigid deformations of subrectangles, are always associated with an increase in required energy, we also include the diagonal edges in each subrectangle (see Figure 1). Now, if we denote the grid coordinates in the source and target images by vectors $\vec{v}_i^{before}, \vec{v}_i^{after}, i \in \{0, 1, \ldots, n_g^2 - 1\}$ and the set of considered edges by E, we can define total energy $U_{total-deform}$ to be minimized as follows:

$$U_{total\text{-}deform} = \sum_{(i,j)\in E} U_{deform}(i,j) \tag{1}$$

where

$$U_{deform}(i,j) = \frac{1}{2} l_{ij} \left(\| \vec{v}_i^{before} - \vec{v}_j^{before} \| - \| \vec{v}_i^{after} - \vec{v}_j^{after} \| \right)^2 \tag{2}$$

where l_{ij} is an elasticity constant associated with the tissue that edge (i, j) crosses.

2.4 Optimization

In theory, the goal now becomes to find the transformation that corresponds to minimal energy while obtaining perfect similarity between the images, i.e. a constrained single-objective optimization problem. However, in practice, due to issues such as noise in image acquisition, inaccuracy in the determination of the parameters of the physical model (i.e. segmentation and values for material properties) and the inability to mathematically compactly represent all possible transformations, a transformation that results in perfect similarity may not exist. Also, in registration tasks to be performed in practice there may be inherent differences between the source and target image that do not correspond to a transformation as a result of deformation only. The source and target images are typically different image acquisitions that may not represent the exact same anatomy. Between acquisitions, physical changes may have occurred such as inflammation, new tumor growth or tumor excision. Furthermore, images may be acquired with different modalities. Moreover, transformations that result in a larger similarity are not necessarily preferable. Therefore, the underlying problem in practice is actually multi-objective, i.e. find transformations that on the one hand maximize the similarity between source and target image (objective 1) and on the other hand minimize the amount of required energy (objective 2).

In this work we therefore take a multi-objective optimization approach. In multi-objective optimization, the optimum is a set of solutions, called the optimal Pareto set, because many solutions may be equally good, e.g. solution a may be better in the first objective than solution b, but worse in the second objective. Solutions in the Pareto set are said to not *dominate* each other. The benefit of using such a methodology is two-fold. First, applying linear combinations (as is typically done in image registration) of the similarity and energy objectives can by definition not find all possible Pareto-optimal solutions.[7] Specifically, concave parts in the optimal Pareto front cannot be found (the Pareto front is the mapping of the solutions in the Pareto set from the solution space to the space of objective values). Second, even if the entire Pareto front, or the part we are interested in, is convex, using a uniform selection of combinations does not automatically lead to a uniform spread of solutions on the Pareto front.

Population-based methods such as evolutionary algorithms (EAs) are among the state-of-the-art in solving multi-objective optimization problems.[7] Due to the use of a population and specialized operators, near-optimal solutions can be found efficiently and well-spread for both concave and convex parts of the Pareto front. We used a particular type of EA, known as EDA (Estimation-of-Distribution Algorithm), that aims to exploit features of a problem's structure in a principled manner via probabilistic modeling.[8–11] This makes this type of EA typically more robust and capable of solving a large class of optimization problems reliably without using any problem-specific knowledge.

The specific EDA we use is called MAMaLGaM-X (Multi-objective AMaLGaM miXture).[12] MAMaLGaM-X uses a population of solutions, selects 35% of the best solutions according to a domination-rank ordering,

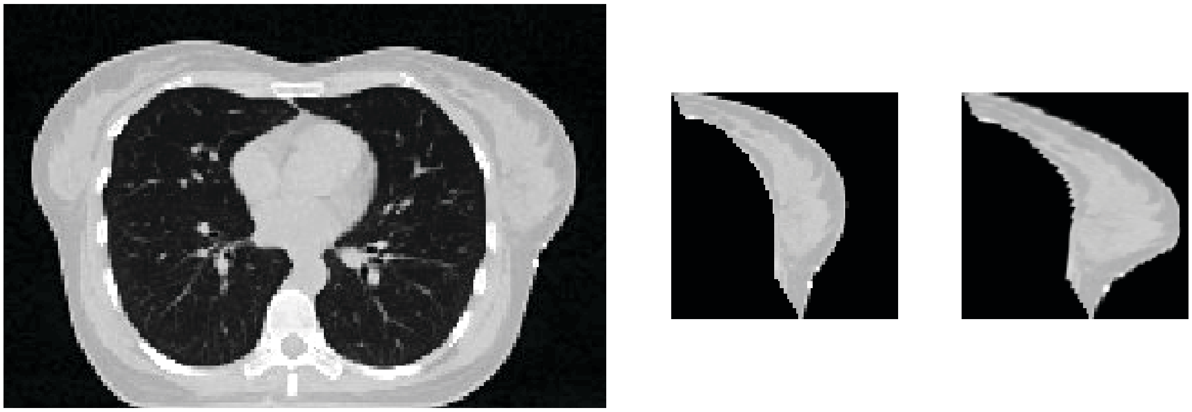

Figure 2. Left: axial slice of a CT scan. Center: segmented left breast (source image). Right: artificially deformed left breast (target image).

estimates a l-dimensional normal mixture distribution (where l is the number of real-valued variables to be optimized) from these selected solutions and generates new solutions by sampling the estimated distribution. Using adaptive techniques that scale the covariance matrices of the normal distributions in the mixture according to improvements found during optimization, the risk of premature convergence is minimized. MAMaLGaM-X was recently demonstrated to be capable of efficiently approximating the optimal Pareto-front on various well-known problems to within a predefined high precision, which can be considered equal to finding the optimum.[12]

The use of such powerful general-purpose optimization algorithms allows us to focus on modeling the problem without compromising model quality due to an increase of model complexity. Such a compromise is otherwise typically necessary because an increase in model complexity can prohibit the design of a problem-specific optimization algorithm. We further used a technique known as constraint domination that allows the definition of constraints in an equally straightforward manner.[13] In this way we could easily incorporate well-known important constraints in deformable registration such as prohibiting transformations that fold the grid.

2.5 Proof of principle

For a proof of principle we selected a 2D slice from a CT image acquired after breast-conserving surgery from a patient suffering from breast cancer. First, the left breast was segmented. The resulting segmented image served as the source image. Next, the target image was created by artificially deforming the segmented breast by use of a different deformation model than what will be used to solve this deformable registration task.

A grid consisting of 25 points (corresponding to $l = 50$ variables for MAMaLGaM-X) was defined on the 2D slice (Figure 3). In this pilot study, we did not further classify the different tissue types in the breast and therefore used only one flexibility value. For the normalized mutual information calculation 16 equal-sized bins between 0 and 255 were used in constructing the histograms that constitute the probability distributions of the grey values in the images.

3. RESULTS

Figure 3 shows a typical Pareto front found by the EDA together with transformed source images for three of the solutions on the Pareto front. The plethora of solutions found by the EDA obtained by running it only once already illustrates one of the advantages that such a method provides. We further note that a small concave part is visible between energy values of approximately 0.2 and 0.3. Although this illustrates how the method is capable of covering concave fronts, it should be noted that this does not necessarily mean that the optimal Pareto front is also partially concave. Overall, although this example is still preliminary, it illustrates plausible and desirable behaviour of the proposed methodology.

In Figure 4, for the three selected solutions, the source, target, transformed source, difference image between target and transformed source image, together with the paired objective values associated with the solution are

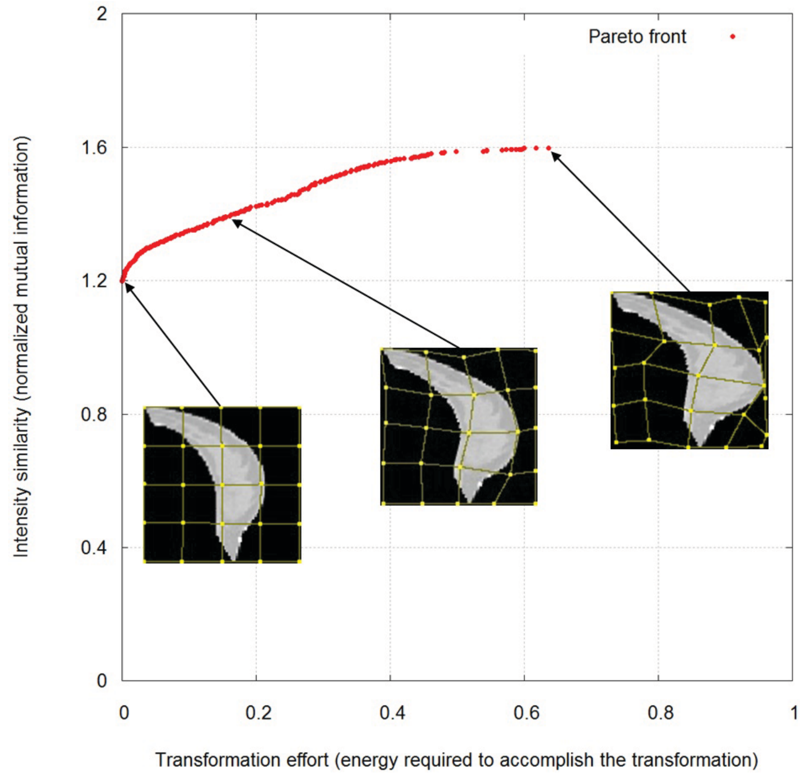

Figure 3. Set of solutions that forms the Pareto front as found by the EDA. For three solutions the corresponding transformed source image is shown. In each image the associated transformed grid is overlaid to give an indication of the extent of the deformation.

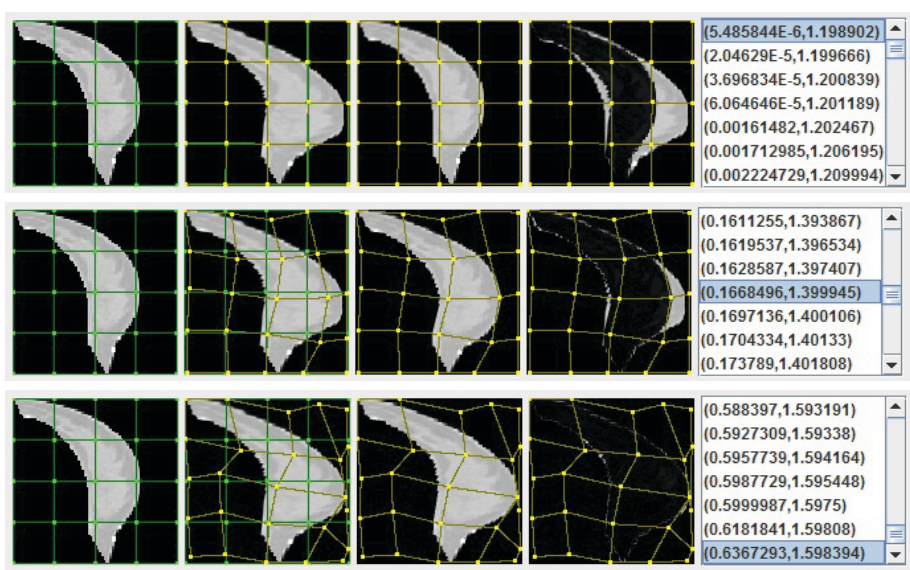

Figure 4. For three solutions from left to right: the source image, the target image, the transformed source image, the difference image between target and transformed source image, the paired objective values associated with the solution (transformation effort, similarity). The three solutions correspond to those presented in Figure 3. The initial regular grid is shown in green. The transformed grid is shown in yellow.

shown. Given the outcomes, it is clear how an expert could now in a transparent manner select the transformation that is considered to be the preferred one. Because the algorithmic search effort is now focused on the entire Pareto front, the diversity that MAMaLGaM-X obtains also includes arguably uninteresting outcomes such as the top example in Figure 4, i.e. for (relatively) small values of deformation energy. It is however fairly straightforward to include expert knowledge in steering the algorithm toward parts of the Pareto front that are more interesting. This allows transformations that are of interest to be found faster and with a higher diversity.

4. DISCUSSION AND CONCLUSION

We present a new approach to deformable image registration based on multi-objective optimization. Existing methods for deformable registration compute the outcome of registration based on a single combination of different objectives. There is however no theoretical basis upon which such a single combination can be optimally selected beforehand. Different combinations lead to different outcomes, which can ultimately only be judged in quality by experts. We employed a multi-objective optimization approach that removes this predetermined singular option in deformable registration. The particular type of multi-objective optimization algorithm that we used is already very efficient, effective and capable of dealing with many different types of problem difficulty which allows us to focus on defining the objectives and constraints such that the registration task is correctly modeled and thereby leads to desired outcomes. The objectives can be easily reformulated as required. In other words, the current model choices (e.g. Hooke's law and normalized mutual information) are not fixed but can be easily varied in our methodology. This can be especially important for future extensions of this work that we are currently working on. For instance, existing deformable registration techniques generally fail to account for anatomical changes (surgery) between image acquisitions. Only a few publications addressed the issue of tissue excision between image acquisitions for the purpose of intra-operative guidance.[14–18] However, in these methods the identification of the disappearing structures is considered a separate task, often as part of segmentation. We consider this challenging problem however to be part of the overall optimization process, thereby letting the optimization algorithm decide and identify which parts are most likely to have (dis)appeared. We believe the additional problem complexity that this introduces can be effectively tackled by the chosen optimization technique.

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