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Biomedical Image Analysis Using Markov Random Fields & Efficient Linear Programing

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Abstract— **Computer-aided diagnosis through biomedical image analysis is increasingly considered in health sciences. This is due to the progress made on the acquisition side, as well as on the processing one. In vivo visualization of human tissues where one can determine both anatomical and functional information is now possible. The use of these images with efficient intelligent mathematical and processing tools allows the interpretation of the tissues state and facilitates the task of the physicians. Segmentation and registration are the two most fundamental tools in bioimaging. The first aims to provide automatic tools for organ delineation from images, while the second focuses on establishing correspondences between observations inter and intra subject and modalities. In this paper, we present some recent results towards a common formulation addressing these problems, called the Markov Random Fields. Such an approach is modular with respect to the application context, can be easily extended to deal with various modalities, provides guarantees on the optimality properties of the obtained solution and is computationally efficient.**

I. INTRODUCTION

Recent developments on the hardware side have led to a new generation of scanners as well as image modalities where the in vivo visualization of anatomical structures of biological systems is possible in a non invasive fashion. The exploitation of such an information space is a great challenge of our days and consists of understanding the anatomical structure of biological systems and in particular the effect of pathologies on their complex mechanisms of operation.

One can consider such a task from a mathematical perspective. In such a case, for a given modeling task the first objective consists of parameterizing the problem or associating the understanding of a complex mechanism through a mathematical model that describes a generic behavior and depends on a number of parameters. Given such a model, the next step aims to establish a relation between the theoretical model and the available observations. In simple words, we should be able to understand the impact of model parameters to the data. Last, but not least, inference of the model parameters given the data is to be performed, or recover the set of values that once applied to the model will optimally explain the data.

There are several challenges in such a process.

- **curse of dimensionality**: ideally a complex model would have excellent capabilities on approximating the organ under observation behavior but it will be hard to infer,
- **curse of non-linearity**: often the observations are not directly associated with the model and therefore there is a non-linear relationship between them that makes inference quite problematic,
- **curse of non-convexity**: in most of the cases the designed cost function is too complex and therefore recovering computationally the optimal solution is not obvious/feasible
- **curse of non-modularity**: in particular as it concerns the data-association and inference steps where the models are hard-encoded in the process, decreasing the modularity of the proposed methods to specific clinical problems and even more specific class of models.

The use of prior knowledge is often considered to reduce the model complexity while preserving its ability to capture the expectable behavior. This is done either through the use of anatomy or through the use of machine learning techniques on an important set of training examples. In order to address the curse of non-linearity, the idea of decomposition between the model and the data association is the most prominent. Such an approach aims to decouple dependencies between the model parameters with the data making possible a better association between them. The non-convexity issue can be addressed either by introducing additional regularization constraints (the objective function becomes convex) or by dropping some of the model constraints towards simplification of the objective function. Last, but not least modularity can be addressed through the use of gradient-free methods.

Markov Random Fields [4] is a popular paradigm in computer vision and medical image analysis. The central idea is to represent the parameter estimation problem through a graph. The connections between graph-nodes exploit the co-dependencies/constraints between the model variables. The inference consists of finding the most appropriate labeling such that the corresponding objective function is minimized. In this paper, we introduce a novel approach to perform inference in biomedical image analysis using MRFs, relaxations and efficient linear programming. The generic formulation and the corresponding optimization methods will be presented in section 2. Medical image analysis problems will be briefly explained in section 3 while the last section will conclude the paper.

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II. MARKOV RANDOM FIELDS AND EFFICIENT LINEAR PROGRAMMING

A wide variety of tasks in medical can be formulated as discrete labeling problems. In very simple terms, a discrete optimization problem can be stated as follows: we are given a discrete set of variables $\mathcal{V}$, all of which are vertices in a graph $\mathcal{G}$. The edges of this graph (denoted by $\mathcal{E}$) encode the variables' relationships. We are also given as input a discrete set of labels $\mathcal{L}$. We must then assign one label from $\mathcal{L}$ to each variable in $\mathcal{V}$. However, each time we choose to assign a label, say, x_p to an object p, we are forced to pay a price according to the so called *singleton* potential function $V_p(x_p)$, while each time we choose to assign a pair of labels, say, x_p and x_q to two interrelated variables p and q (two objects that are connected to each other by an edge in the graph $\mathcal{G}$), we are also forced to pay another price, which is now determined by the so called *pairwise* potential function $V_{pq}(x_p, x_q)$ (both the singleton and pairwise potential functions are problem specific and are thus assumed to be provided as input).

Our goal is then to choose a labeling which will allow us to pay the smallest total price. In other words, based on what we have mentioned above, we want to choose a labeling that minimizes the sum of all the MRF potentials, or equivalently the MRF energy. This amounts to solving the following optimization problem:

$$\arg\min_{\{x_p\}} \sum_{p \in \mathcal{V}} V_p(x_p) + \sum_{(p,q) \in \mathcal{E}} V_{pq}(x_p, x_q). \qquad (1)$$

The use of such a model can describe a number of challenging problems in medical image analysis. Parameters inference is the most critical aspect in computational medicine and efficient optimization algorithms are to be considered both in terms of computational complexity as well as of inference performance. Discrete MRFs are a very promising framework that assumes local/limited interactions between the model variables. Such a paradigm can be used to efficiently model a number of problems in medical imaging, like denoising, enhancement, feature extraction, segmentation, shape alignment, registration, etc. However, most of the existing methods were constrained from the type of interactions that one can introduce between the model variables. The use of relaxation techniques, linear programming and duality are a prominent direction to deal with the minimization of generic MRFs.

A. LP-Relaxations and Primal Dual Method

In [11] we introduced a novel method to address minimization of static and dynamic MRFs. Our approach is based on principles from linear programming and, in particular, on primal dual strategies. It generalizes prior state-of-the-art methods such as α-expansion, while it can also be used for efficiently minimizing NP-hard problems with complex pairwise potential functions. Furthermore, it offers a substantial speedup - of a magnitude ten - over existing techniques, due to the fact that it exploits information coming not only from the original MRF problem, but also from a dual one. The proposed technique consists of recovering pair of solutions for the primal and the dual such that the gap between them is minimized. Therefore, it can also boost performance of dynamic MRFs, where one should expect that the new new pair of primal-dual solutions is closed to the previous one.

B. Master-Slave Decomposition and Message Passing

In [8] a new message-passing scheme for MRF optimization was proposed. This scheme inherited better theoretical properties than all other state-of-the-art message passing methods and in practice performed equally well/outperformed them. It is based on the very powerful technique of Dual Decomposition [1] and leads to an elegant and general framework for understanding/designing message-passing algorithms that can provide new insights into existing techniques. Promising experimental results and comparisons with the state of the art demonstrated the extreme theoretical and practical potentials of our approach.

C. Tighter LP-Relaxations and Cycle Repairing

In [7] we have focused our attention on MRFs problems where the relaxation is known to be loose, or the solution of the relaxed problem is not optimal for the original one. We have introduced a novel generic solver that it does so by relying on a much tighter class of LP-relaxations, called cycle-relaxations. With the help of this class of relaxations, our algorithm tries to deal with a difficulty lying at the heart of MRF optimization: the existence of inconsistent cycles. To this end, it uses an operation called cycle-repairing. The goal of that operation is to fix any inconsistent cycles that may appear during optimization, instead of simply ignoring them as usually done up to now. The more the repaired cycles, the tighter the underlying LP relaxation becomes. As a result of this procedure, our algorithm is capable of providing almost optimal solutions even for very general MRFs with arbitrary potentials.

D. LP-Relaxations and Higher Order MRFs

In [10] towards addressing MRFs of higher order with arbitrary dependencies between the model variables we have introduced a novel optimization approach to derive an optimizer. The method can be applied to almost any higher-order MRF and optimizes a dual relaxation related to the input MRF problem. Such a generic approach is extremely flexible and thus can be easily adapted to yield far more power algorithms when dealing with subclasses of high-order MRFs. We introduced a new powerful class of high-order potentials, which are shown to offer enough expressive power and to be useful for many vision tasks. In order to address them, we derived a novel and extremely efficient message-passing algorithm, which goes beyond the aforementioned generic optimizer and is able to deliver almost optimal solutions of very high quality.

III. MEDICAL IMAGE ANALYSIS AND COMPUTER AIDED DIAGNOSIS

One can now combine the theoretical model with the efficient optimization techniques towards computer-aided diagnosis. Segmentation and registration are among the most fundamental problems in medical imaging. Knowledge-based segmentation consists of automatic delineation of a structure of interest from an image being constrained from certain shape priors. The objective of image fusion is to determine a transformation that will allow direct comparison of measurements coming from the same or different modalities etc. Such a technology facilitates clinical diagnosis and better understanding of the effects of different diseases.

A. Image Segmentation

In [2] and [3], we introduced a new approach to knowledge-based segmentation. Our method consists of a novel representation to model shape variations as well as an efficient inference procedure to fit the model to new data.

The shape model: The considered shape model is similarity-invariant and refers to a graph where the nodes $p \in \mathcal{V}$ represent control points and where the edges $(p, q) \in \mathcal{E}$ represent the dependencies between them. These dependencies are determined accorind to the normalized Euclidean distances d_{pq} between the connected control points. With this modeling, we introduce a prior knowledge about the shape variations by learning the probability density distributions $Pr(d_{pq})$ of the relative positions of the control points, using a training set of labeled shapes. The idea behind this model is to deform the surface of the object by displacing the control points in a way that is consistent with the learned prior constraints.

The graph structure: Defining the graph structure by thoroughly selecting a subset of connections between nodes is an important issue to achieve a sparse representation that is computationally efficient on one hand, and that does not suffer from redundancy on the other hand. Therefore, we construct an incomplete graph that consists of intra and inter-cluster connections that represent the inter-dependencies of the control points. We first determine the clusters according to the co-dependencies of the deformations of the control points within the training set. Shape maps [12] provide an embedding into a manifold where the Euclidean distance describes the latter criterion. A new linear-programming-based clustering algorithm [9] is then used to determine the clusters as well as their number. Then, the connections between the components of a cluster represent the local structure while the connections between the clusters account for the global structure. The distributions of the normalized distances between these connections encode the prior model as stated previously.

Model-based segmentation: During search, this model was used in a MRF framework (1), where the unknown variables x_p are the positions of the control points in the image domain. To encode the image support, we considered a Voronoi decomposition of the domain and used region-based statistics. Hence, the singleton potentials $V_p(x_p)$ evaluate from the image point of view the local deformation of the model by displacing the control point p to the position x_p. The prior knowledge is encoded in the pairwise potentials $V_{pq}(x_p, x_q)$ that express the cost of deforming the connection (p, q) (of the incomplete learned graph) to the new positions x_p and x_q, with respect to the learned distributions $Pr(d_{pq})$. The resulting model is computationally efficient, can encode complex statistical models of shape variations and benefits from the image support of the entire spatial domain. Some experimental results with respect to the segmentation of the left ventricle in 3D CT images are shown in [Fig. (1)].

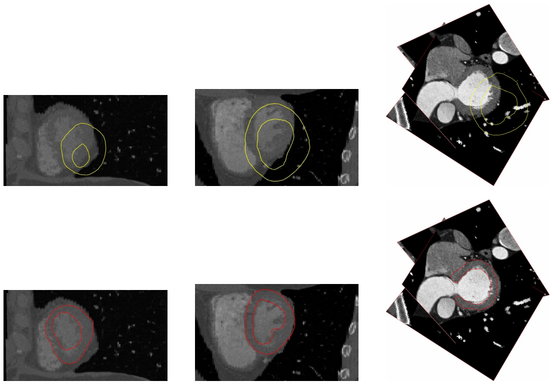

Fig. 1: Demonstrative Segmentation results for 3D CT Cardiac Data: (top) initial conditions, (bottom) obtained segmentation results.

B. Image Registration

In [5] we introduced a novel and efficient approach to dense image registration, which does not require a derivative of the employed cost function. In such a context the registration problem was formulated using a discrete Markov Random Field objective function. Considering the common approach of energy minimization for the registration of two images I and J

$$T^* = \arg\min_{T} \phi\left(I, J \circ T\right) \quad , \tag{2}$$

one seeks for recovering the optimal transformation T^* w.r.t. a similarity measure ϕ such that the two images are perfectly aligned. The new location of an image point $\mathbf{x}$ can be depicted from the transformation $T(\mathbf{x}) = \mathrm{Id}(\mathbf{x}) + D(\mathbf{x})$ which consists of the identity transformation $\mathrm{Id}(\mathbf{x}) = \mathbf{x}$ and a dense displacement field $D(\mathbf{x}) = \Delta\mathbf{x}$.

Towards dimensionality reduction on the variables we assume that the dense displacement field can be expressed using a small number of control points (registration grid) and an interpolation strategy [13]. The displacement of an image point can then be computed by a linear combination of the displaced control points p, or

$$\Delta\mathbf{x} = \sum_{i=1}^{M} \eta(\mathbf{x})\, \Delta p_i \quad , \tag{3}$$

where M is the number of control points, Δp_i is the displacement vector of the i-th control point, and η being the interpolation function (often based on B-spline basis functions).

Then, the registration cost is expressed using a discrete sum over image costs (using an arbitrary similarity measure) projected on the control points

$$E_{\text{similarity}}(T) = \sum_{i=1}^{M} \phi_i \left(I, J \circ T\right) \quad . \tag{4}$$

Here, ϕ_i plays the role of a local similarity measure evaluated only in the influence area of an control point determined by the interpolation function η.

Additionally, a smoothness term is considered that penalizes local deviations on the displacement field according to the neighborhood system $\mathcal{E}$ of the registration grid. Assuming that neighboring control points should undergo similar movements, one can for instance penalize the squared difference of the displacement vectors. The key idea in our approach is now to reformulate the registration problem as a discrete MRF labeling problem. Based on the previous definitions, the control points of the registration grid are considered as the discrete variables $\mathcal{V}$. Additionally, the discrete set of labels $\mathcal{L} = \{x_1, ..., x_i\}$ corresponds to a quantized version of the displacement space $\Theta = \{\mathbf{d}_1, ..., \mathbf{d}_i\}$. A label assignment x_p to a grid node p is associated with displacing the node by the corresponding vector $\mathbf{d}_{x_p}$. Based on the general MRF energy, we encode the image costs of the registration problem through the singleton potential functions while the smoothness term is encoded through the pairwise potential functions.

In order to account for large deformations and produce results on a high resolution level a multi-scale incremental approach is considered where the optimal solution is iteratively updated. This is done through successive warping of the source image J towards the target image I on different image and grid resolutions. Simultaneously, the capture range of the quantized displacement space is successively refined. Efficient linear programming using the primal dual principles was considered to recover the lowest potential of the cost function. Towards addressing the main limitation of the discrete optimization methods that is the quantization of the search space, in [6] we have proposed the use of uncertainties to locally determine the range of the search space. Some experimental results with respect to this application are shown in [Fig. (2)].

IV. DISCUSSION

In this paper we have presented a generic methodological framework as well as the corresponding inference method to address medical image analysis. We have opted for the use of Markov Random Fields and efficient linear programming. Such an approach addresses most of the challenges of biomedical image analysis. It can cope with an important number of problems, can deal with the non-linearity, the non-convexity and is gradient-free and modular. Two of the most important problems in the field of medical image analysis were considered to demonstrate the potentials of this method, that were the problems of segmentation and registration.

The use of models involving higher order variables interactions is the most promising direction of our work. Modeling biological behaviors often requires interactions between significant number of model variables and the pairwise model is not the most adequate choice. Furthermore, exploring the same methodologies to address feature extraction, data structuring, dimensionality reduction and unsupervised clustering could be beneficial to a number of problems in medical image analysis.

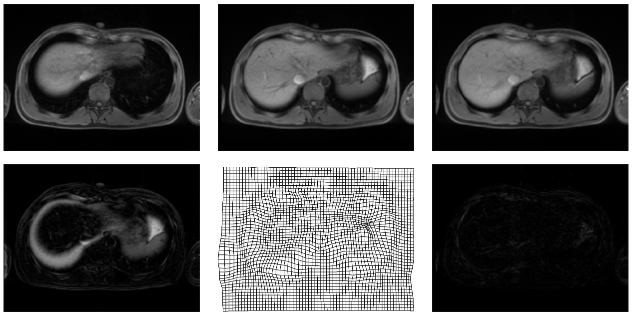

Fig. 2: Registration results for 3D MRI data of two different phases of the breathing cycle. **Top:** on the left the target image (inhalation), on the center the source image (exhalation) and on the right the the warped source image after registration. **Bottom:** on the left the difference image before, on the center the corresponding deformation field and on the right after registration.

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