INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET EN AUTOMATIQUE

Team galen

Organ Modeling through Extraction, Representation and Understanding of Medical Image Content

Saclay - Île-de-France

Theme : Computational Medicine and Neurosciences

Activity Report

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2. Overall Objectives

2.1. GALEN@Ecole-Centrale

Life expectancy in the development and developing countries is keeping increasing. This is due progress made in medicine since now we are able to cure diseases that were considered incurable in the past. Medicine has benefited from progress made on understanding the pattern of diseases and therefore developing the appropriate drugs as well as early novel means for screening and diagnosis at an early stage and therapy treatment evaluation. Biomedical imaging is one of the most promising means of early diagnosis at least for a number of diseases. Medical hardware manufacturer's progress has lead to a new generation of measurements towards understanding the human anatomical and functional state. These measurements go beyond simple means of anatomical visualization (e.g. X-ray images) and therefore their interpretation becomes a scientific challenge for humans mostly because of the volume and the flow of information as well as their nature.

Computer-aided diagnosis aims at developing mathematical models and their computational solutions to assist data interpretation in a clinical setting. In simple words, one would like to be able to provide a formal answer to a clinical question using the available measurements. The development of mathematical models for automatic clinical interpretation of multi-modalities is a great challenge. The mathematical formulation of clinical data interpretation aims to introduce a compact set of parameters that are to be inferred from the data and answer the clinical question. Such a task requires a consensus between physicians and applied mathematicians, towards the definition of a feasible, clinically-interesting model. Once this model has been defined, the next task consists of associating it with the available observations that also requires the establishment of an anatomical/physiological interpretation of its components with respect to the measurements. Last, one has to computationally solve the inference problem, or among the set of parameters expressing the model, which do optimally interpret the data. This simplistic description of biomedical inference makes clear that it is an inter-disciplinary effort that requires synergies between medicine, applied mathematics, machine learning, statistical modeling and optimization.

Despite enormous progress made on the field of biomedical image analysis still a huge gap exists between clinical research and clinical use. The aim of GALEN is three-fold. First we would like to introduce a novel biomedical image perception framework for clinical use towards disease screening and drug evaluation. Such a framework is expected to be modular (can be used in various clinical settings), computationally efficient (would not require specialized hardware), and can provide a quantitative and qualitative anatomo-pathological indices. Second, leverage progress made on the field of machine learning along with novel, efficient, compact representation of measurements toward computer aided diagnosis. Last, using these emerging multi-dimensional signals, we would like to perform longitudinal modeling and understanding the effects of aging to a number of organs and diseases that do not present pre-disease indicators such as brain neurological diseases, muscular diseases, certain forms of cancer, etc.

GALEN aims at proposing innovative techniques towards automatic structuring, interpretation and longitudinal modeling of medical measurements through the analysis of anatomical and functional images. In order to address these fundamental problems of biomedical perception, GALEN investigates the use of discrete models of varying complexity. These methods exhibit an important number of strengths such as their ability to be modular with respect to the input measurements (clinical data), the nature of the model (certain constraints are imposed from computational perspective in terms of the level of interactions), and the model-to-data association while being computational efficient. Successful completion of the above efforts will lead to better understanding of organ evolution due to aging and will provide novel means of diagnosis, follow up, and therapy treatment evaluation. Long-term modeling and understanding the effects of aging is critical to a number of organs and diseases that do not present pre-disease indicators like brain neurological diseases, muscular diseases, certain forms of cancer, etc.

2.2. Highlights

ERC-Starting Grant/Consolidator: GALEN was attributed a grant from the European Research Council towards building a Discrete Biomedical Perception Paradigm towards Computer Aided Diagnosis and Longitudinal Organ Modeling.

Annual Review of Biomedical Engineering: The Annual Review of Biomedical Engineering covers the significant developments in the broad field of Biomedical Engineering. Papers are by invitation only and the journal is among the highest impact factor journals in the field. GALEN's work on deformable image fusion using discrete optimization methods was invited to contribute to the 2011 edition.

ISBI Best Student Paper Award: GALEN was the recipient through A. Sotiras of the best student paper award for the following contribution: *A. Sotiras, R. Neji, J-F. Deux, N. Komodakis, G. Fleury & N. Paragios. A Kernel-based Graphical Model for Diffusion Tensor Registration*.

CVPR Participation: GALEN has participated in the 2010 annual IEEE Conference in Computer Vision and Pattern Recognition (CVPR'10) conference, the leading event in the field of computer vision and medical image analysis with five papers (double blind full submissions, acceptance rate %25) including one oral presentation (out of a 60).

MICCAI Participation: GALEN has participated in the 2010 annual Medical Image Computing and Computer Assisted Intervention (MICCAI'10) conference one of the leading events in the field of medical image analysis with five (double blind full submissions, acceptance rate %35).

ISBI Participation: GALEN has participated in the 2010 International Symposium of Biomedical Imaging (ISBI'10) conference, one of the notable events in the field of medical image analysis with seven papers (acceptance rate %40) including three oral presentations.

3. Scientific Foundations

3.1. Discrete Biomedical Image Perception

A wide variety of tasks in medical image analysis 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_1} to a variable p_1, we are forced to pay a price according to the so-called *singleton* potential function $g_p(x_p)$, while each time we choose to assign a pair of labels, say, x_{p_1} and x_{p_2} to two interrelated variables p_1 and p_2 (two nodes that are connected 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 $f_{p_1p_2}(x_{p_1}, x_{p_2})$. 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:

$$\arg\min_{\{x_p\}} \mathcal{P}(g,f) = \sum_{p\in\mathcal{V}} g_p(x_p) + \sum_{(p_1,p_2)\in\mathcal{E}} f_{p_1p_2}(x_{p_1}, x_{p_2}). \tag{1}$$

The use of such a model can describe a number of challenging problems in medical image analysis. However these simplistic models can only account for simple interactions between variables, a rather constrained scenario for high-level medical imaging perception tasks. One can augment the expression power of this model through higher order interactions between variables, or a number of cliques $\{C_i, i\in[1,n] = \{\{p_{i^1},\cdots,p_{i^{|C_i|}}\}\}$ of order $|C_i|$ that will augment the definition of $\mathcal{V}$ and will introduce hyper-vertices:

$$\arg\min_{\{x_p\}} \mathcal{P}(g,f) = \sum_{p\in\mathcal{V}} g_p(x_p) + \sum_{(p_1,p_2)\in\mathcal{E}} f_{p_1p_2}(x_{p_1}, x_{p_2}) + \sum_{C_i\in\mathcal{E}} f_{p_1\cdots p_n}(x_{p_{i^1}},\cdots,p_{x_{i^{|C_i|}}}). \tag{2}$$

where $f_{p_1\cdots p_n}$ is the price to pay for associating the labels $(x_{p_{i^1}},\cdots,p_{x_{i^{|C_i|}}})$ to the nodes $(p_1\cdots p_{i^{|C_i|}})$. Parameter inference, addressed by minimizing the problem above, is the most critical aspect in computational medicine and efficient optimization algorithms are to be evaluated both in terms of computational complexity as well as of inference performance. State of the art methods include deterministic and non-deterministic annealing, genetic algorithms, max-flow/min-cut techniques and relaxation. These methods offer certain strengths while exhibiting certain limitations, mostly related to the amount of interactions which can be tolerated among neighborhood nodes. In the area of medical imaging where domain knowledge is quite strong, one would expect that such interactions should be enforced at the largest scale possible; however this is not supported by the existing state-of-the art methods.

3.1.1. Linear Programming, Loose Relaxations & Duality

The binary MRF case, considering the optimization of Eq. 2 for binary variables, has been well studied from the optimization community. The main challenge is to find a computational efficient solution that provides a good compromise between the convergence time and the optimality properties of the solution. To this end, we have introduced a novel method [6], called Fast-PD that outer performs the state of the art from theoretical point of view (classes of energies which can be considered) as well as from computational perspective (five to ten times faster). This is an optimization technique, which builds upon principles drawn from the duality theory of linear programming in order to efficiently derive almost optimal solutions for a very wide class of NP-hard MRFs.

3.1.2. Tight Relaxations, Cycle Repairing & Duality

Despite their success, LP-based methods are doomed to fail if relaxation does not approximate well the actual problem MRF (*i.e*, it is not tight), which is exactly what happens when one has to deal with very hard MRF problems. We believe this is an issue that has to be addressed, if a further advance is to be made in MRF optimization. In [4] we have attempted to go beyond most existing MRF techniques, by deriving algorithms that are based on much tighter LP relaxations. Towards this goal, we try to strengthen the relaxation in the dual domain. As a result, we create a hierarchy of increasingly tighter dual relaxations, going all the way up to a dual relaxation that actually coincides with the original problem MRF. This is a novel LP-based algorithm for MRF optimization, which, contrary to most state-of-the-art techniques, no longer relies on a weak LP-relaxation. To this end, we have shown how one can take advantage of a very tight class of relaxations from our increasingly tighter hierarchy, named cycle-relaxations. This is done through an operation called cycled repairing, where inconsistent cycles get repaired during optimization.

3.1.3. Master-Slave Decompositions, Message Passing and Higher-Order MRFs

MRF inference is extremely popular in medical imaging and related fields. However, with a few exceptions only, its use was mainly confined to the case of pair wise MRFs up to now. One reason is because optimization of higher order MRFs can be extremely difficult (*i.e*, algorithms that yield almost optimal solutions are hard to get in this case) and, furthermore, these algorithms often have a very high computational cost that is prohibitive in practice. Yet, many medical imaging problems could greatly benefit from the use of higher order models as this would allow far more expressive priors to be encoded, and also multiple interactions to be captured. This would, in turn, lead to a far better and more accurate modeling, which is clearly needed by many vision tasks (*e.g*, notice that in many cases there is a large disagreement between the global optimum, that can often be computed for pair wise MRFs and the ground truth). Towards dealing with the above issues, we proposed in [16] a powerful framework for high-order MRF optimization. It uses a *master-slave* based scheme which relies on the core idea that even a hard high-order MRF problem (with, *e.g*, large cliques or complicated structure) can often be decomposed into high-order MRF sub problems that are very easy or even trivial to solve.

3.2. GALEN Research Axes

Medical image perception is a relative recent research field that during the past two decades has focused on the development of mathematical models and their computational solutions towards automatic multi-dimensional signal interpretation. Such an interpretation consists of three levels, namely (i) the "feature" extraction part, (ii) the "anatomical/pathological" interpretation of these "features", and (iii) the longitudinal modeling of observations toward virtual anatomy and disease progress modeling. Despite enormous progress made in the field, significant advances are mostly made on the first level of processing. However, even in that case the most state-of-the art solutions are clinical-application specific and therefore portability into other settings is not possible. More recently, one can also observe a shift to the second level as a side benefit of the emergence of the machine learning discipline. Last, but not least with very few exceptions, the third level of processing has been ignored because of the fact that is extremely challenging from mathematical perspective.

The scientific objectives of GALEN are the following:

3.2.1. Biomedical Image Perception/Interpretation

Introduce a novel, modular (in terms of clinical applications, mathematical perception models and bio-imaging signals), and computational efficient inference framework for biomedical image perception to address the most fundamental problems of medical imaging. Such an approach will facilitate the development of computer-aided diagnosis for every-day clinical use (opposite to clinical research purposes that is mostly the case in now-days). Successful completion of this effort will require the development of novel, efficient, discrete modeling, optimization and inference techniques that could impact a number of domains.

3.2.2. Data Mining of Anatomical and Pathological Biomarkers

Exploit recent advances and introduce novel machine learning techniques for mining of anatomical and pathological biomarkers towards computer-aided diagnosis. In particular, we will focus on novel efficient means for modular unsupervised clustering (in terms of clinical applications, mathematical perception models and bio-imaging signals) towards capturing the most prominent biomedical signals of various diseases. Furthermore, we will look on efficient dimensionality reduction methods that will induce to the classification process the ability to learn from small training sets, one of the most important constraints of data mining.

3.2.3. Longitudinal Organ Modeling

Propose organ "‘progression"’ models that account for aging through inference from multi-dimensional bio-imaging signals. To this end, we imagine a set of subjects being imaged with a certain frequency non-invasively. Longitudinal modeling aims at automatic interpretation using non-linear time series that couple anatomical and pathological indices. Such an approach will provide: (i) a better understanding of the aging process, (ii) means of recovering risk factors for certain diseases at very early stage, (iii) means of diagnosis for long-term pathologies without pre-clinical symptoms. This will be of particular challenge when focusing either on children (where one observes rapid, and unknown to a certain extent evolution in number of organs), or adults being affected with diseases of unknown temporal signature.

3.3. Clinical Projects at Glance

Participants: Hugues Duffaut, Phillipe Grenier, Valery Trosini-Desert, Thomas Similowski, Nikos Paragios.

- **Machine Learning, Deformable Registration and Virtual Bronchoscope**: [APHP Pitie SalPetriere]: The technological advance introduced by the flexible bronchoscope dates back to the 1960s. Flexible bronchoscopy rapidly became a recognized diagnostic method and one of the standard diagnostic techniques in chest medicine. It is used for diagnostic procedures as well as therapeutic ones. The idea behind such a project is to be able to perform real-time multi-modal alignment between preoperative annotated data (CT) and interventional data bronchoscope images. Such a process will lead to an automatic navigation tool on the 3D bronchial topography model obtained through preoperative procedures. Therefore it will allow physicians to perform better diagnosis as well as better treatment of diseases.
- **Detection, Segmentation and Inference on Spatial Position Understanding of Low-grade Gliomas Brain Tumors**: [CHU Montpellier]: Low-grade gliomas (WHO grade II) are diffusively infiltrative brain tumors arising from glial cells. Spatial classification of WHO grade II gliomas is usually based on cerebral lobes. This kind of classification lacks accuracy and is far from being able to provide some pattern or statistical interpretation of their appearance. The aim of this study is twofold. First, we would like to develop an automatic tumor segmentation method that will be able to detect low-grade gliomas automatically. The second objective is to infer a statistical representation guiding/explaining the intra-brain geometric behavior of the gliomas across individuals. Such information can be a valuable tool towards better and more precise early diagnosis as well as surgery planning.

4. Software

4.1. Deformable Registration Software

Participants: Nikos Paragios [Correspondant], Ben Glocker, Aristeidis Sotiras, Nikos Komodakis.

DROP is a deformable registration platform in C++ for the medical imaging community (publicly available at http://www.mrf-registration.net) developed mainly at Ecole Centrale, Technical University of Munich and University of Crete. This is the first publicly available platform which contains most of the existing metrics to perform registration under the same concept. The platform is used for clinical research from approximately 2,000 users worldwide.

4.2. Fast Primal Dual Strategies for Optimization of Markov Random Fields

Participants: Nikos Komodakis [Correspondant], Nikos Paragios, George Tziritas.

FASTPD is an optimization platform in C++ for the computer vision and medical imaging community (publicly available at http://www.csd.uoc.gr/~komod/FastPD/) developed mainly at Ecole Centrale and University of Crete. This is the most efficient publicly available platform in terms of a compromise of computational efficiency and ability to converge to a good minimum for the optimization of generic MRFs. The platform is used from approximately 1,000 users worldwide.

4.3. Texture Analysis Using Modulation Features and Generative Models

Participants: Iasonas Kokkinos [Correspondant], Georgios Evangelopoulos.

TEXMEG is a front-end for texture analysis and edge detection platoform in Matlab that relies on Gabor filtering and image demodulation (publicly available at http://cvsp.cs.ntua.gr/software/texture/). Includes frequency- and time- based definition of Gabor- and other Quadrature-pair filterbanks, demodulation with the Regularized Energy Separation Algorithm and Texture/Edge/Smooth classification based on MDL criterion.

5. New Results

5.1. Discrete Optimization Using Dual Decomposition

Participants: Nikos Komodakis, Nikos Paragios.

In [16] we introduced a new rigorous theoretical framework to address discrete MRF-based optimization in medical imaging that exploits Dual Decomposition. The method was based on a projected sub gradient scheme that attempts to solve an MRF optimization problem by first decomposing it into a set of appropriately chosen sub problems and then combining their solutions in a principled way. In order to determine the limits of this method, we analyze the conditions that these sub problems have to satisfy and we demonstrate the extreme generality and flexibility of such an approach. We have shown that, by appropriately choosing what sub problems to use, one can design novel and very powerful MRF optimization algorithms. Theoretical analysis on the bounds related with the different algorithms derived from our framework and experimental results/comparisons using synthetic and real data for a variety of tasks in computer vision and medical imaging demonstrated the extreme potentials of our approach.

5.2. Reconstruction of Spatio-temporal Signals

Participants: Noura Azzabou, Nikos Paragios.

In [12] we proposed a novel variational framework for speckle removal in ultrasound images. Our method combines efficiently a fidelity to data term adapted to the Rayleigh distribution of the speckle and a novel spatio-temporal smoothness constraint. The regularization relies on a non parametric image model that describes the observed image structure and expresses inter-dependencies between pixels in space and time. The interaction between pixels is determined through the definition of new measure of similarity between them to better reflect image content. To compute this similarity measure, we take into consideration the spatial aspect as well as the temporal one.

5.3. Shape Representations, Matching and Modeling

Participants: Yun Zheng, Chaohui Wang, Georg Langs, Dimitris Samaras, Nikos Paragios.

- **Joint Geometry and Appearance Modeling** The learning of the shape and appearance behavior of complex anatomical structures is of growing importance in the successful use of medical imaging data. In [17] we proposed a method to simultaneously learn a model of shape variation and the behavioral structure of objects in volumetric data sets. The method was based on an emerging model of the shape variation, which is learned autonomously from a gated computed tomography sequence. It automatically adapts to the highly non-uniform elasticity properties of the structure during learning. The resulting deformation model was used for the measurement of global and local characteristics of the endograft movement.
- **Higher Order Graph Matching** In [35] we proposed a high-order graph matching formulation to address non-rigid surface matching. The singleton terms capture the geometric and appearance similarities (e.g., curvature and texture) while the high-order terms model the intrinsic embedding energy. The novelty of this paper includes: 1) casting 3D surface registration into a graph matching problem that combines both geometric and appearance similarities and intrinsic embedding information, 2) the first implementation of high-order graph matching algorithm that solves a non-convex optimization problem, and 3) an efficient two-stage optimization approach to constrain the search space for dense surface registration.

5.4. Rigid & Deformable Image Fusion/Registration

Participants: Ben Glocker, Fabrice Michel, Yangming Ou, Aristeidis Sotiras, Alex Bronstein, Michael Bronstein, Nikos Komodakis, Christos Davatzikos, Nikos Paragios.

- **Metric Learning** in [28] we introduced a novel approach for metric learning, aiming to address highly non functional correspondences through the integration of statistical regression and multi-label classification. We developed a position-invariant method that models the variations of intensities through the use of linear combinations of kernels that are able to handle intensity shifts. Such transport functions are considered as the singleton potentials of a Markov Random Field (MRF) where pair-wise connections encode smoothness as well as prior knowledge through a local neighborhood system. We used recent advances in the field of discrete optimization towards recovering the lowest potential of the designed cost function.
  Furthermore, in [20] we introduced a generic framework for supervised similarity learning based on embedding the input data from two arbitrary spaces into the Hamming space. The mapping was expressed as a binary classification problem with positive and negative examples, and can be efficiently learned using boosting algorithms. The utility and efficiency of such a generic approach was demonstrated for the case of alignment of multi-modal medical images.
- **Linear Registration** in [19], [36] we proposed a framework for intensity-based registration of images by linear transformations, based on a discrete Markov random field (MRF) formulation. This formulation was based on a transformation of a high-order MRF model into a tractable second-order one. We demonstrate the quality of the proposed approximation by computing the correlation with the original energy, and show that registration can be performed by discrete optimization of the approximated energy in an iteration loop. A search space refinement strategy was employed over

iterations to achieve sub-pixel accuracy, while keeping the number of labels small for efficiency. The proposed framework can encode any similarity measure is robust to the settings of the internal parameters, and allows an intuitive control of the parameter ranges.

- **Deformable Landmark and Iconic Registration** In [29], [8] we presented a framework for extracting mutually salient landmark pairs for registration. Our method detected landmarks pair-by-pair across images, and those pairs are required to be mutually-salient, i.e., uniquely corresponding to each other. The second merit of our framework was that, instead of finding individually optimal correspondence, which is a local approach and could cause self-intersection of the resultant deformation, our framework adopts a Markov-random-field (MRF)-based spatial arrangement to select the globally optimal landmark pairs. In this way, the geometric consistency of the correspondences is maintained and the resultant deformations are relatively smooth and topology-preserving.
  Such a concept was integrated to iconic registration (that was evaluated in the context of Thoracic CT Images in [37]) in [33], [14] where we introduced a novel approach to bridge the gap between the landmark-based and the iconic-based voxel-wise registration methods. The registration problem was formulated with the use of Markov Random Field theory resulting in a discrete objective function consisting of thee parts. The first part of the energy accounts for the iconic-based volumetric registration problem while the second one for establishing geometrically meaningful correspondences by optimizing over a set of automatically generated mutually salient candidate pairs of points. The last part of the energy penalizes locally the difference between the dense deformation field due to the iconic-based registration and the implied displacements due to the obtained correspondences.
  Furthermore, in [18] a general-purpose deformable registration algorithm referred to as "DRAMMS" was presented with primarily two contributions. First, DRAMMS renders each voxel relatively distinctively identifiable by a rich set of attributes, therefore largely reducing matching ambiguities. A second contribution of DRAMMS is that it modulates the registration by assigning higher weights to those voxels having higher ability to establish unique (hence reliable) correspondences across images, therefore reducing the negative impact of those regions that are less capable of finding correspondences (such as outlier regions). As a result, voxels do not contribute equally as in most voxel-wise methods, nor in isolation as in landmark/feature-based methods. Instead, they contribute according to the continuously-valued mutual-saliency map, which dynamically evolves during the registration process.
- **Mutli-modal and High-dimensional Deformable Fusion** In [31], [11] we introduced a novel approach to perform cinematic and optical imaging fusion towards enhancement of the biological signal. To this end, fusion was reformulated as a population (all vs. all) registration problem where the two (being spatially aligned) signals are registered in time using the same deformation field. Implicit silhouette and landmark matching are considered for the cinematic images and are combined with global statistical congealing-type measurements of the optical one. The problem is reformulated using a discrete MRF; where optical imaging costs are expressed in singleton (global) potentials, while smoothness constraints as well as cinematic measurements through pair-wise potentials.
  The same principles were used for the spatial normalization of diffusion tensor images [32], [10]. The proposed method took advantage of both the diffusion information and the spatial location of tensor in order to define an appropriate metric in a probabilistic framework. A registration energy was defined in a Reproducing Kernel Hilbert Space (RKHS), encoding the image dissimilarity and the regularity of the deformation field in both the translation and the rotation space. The problem was reformulated as a graphical model where the latent variables are the rotation and the translation that should be applied to every tensor and the observed variables are the tensors themselves. Efficient linear programming was used to minimize the resulting energy in both of the above cases.

5.5. Low-level, Model-free & Model-based Segmentation

Participants: Nicolas Honnorat, Fabrice Michel, Chaohui Wang, Iasonas Kokkinos, Nikos Paragios.

- **Low-level Grouping** In [26] a method for accurate boundary detection and grouping was proposed. We first pursued a learning-based approach to boundary detection. For this (i) we leveraged appearance and context information by extracting descriptors around edgels and use them as features for classification, (ii) we used discriminative dimensionality reduction for efficiency and (iii) we used outlier-resilient boosting to deal with noise in the training set. We then introduce fractional-linear programming to optimize a grouping criterion that was expressed as a cost ratio.
  This method was further improved in [27] where a boosting-based approach to boundary detection was considered. To achieve this we introduced the following novel ideas: (a) we use a training criterion that approximates the F-measure of the classifier, instead of the exponential loss that is commonly used in boosting. We optimized this criterion using Anyboost. (b) We dealt with the ambiguous information about orientation of the boundary in the annotation by treating it as a hidden variable, and train our classifier using Multiple-Instance Learning. (c) We adapted the Filterboost approach to leverage information from the whole training set to train our classifier, instead of using a fixed subset of points. (d)We extracted discriminative features from appearance descriptors that are computed densely over the image.
- **Mid-level Grouping** Towards high-level interpretation of boundary-detection measurements, in [15] we introduced a hierarchical representation for object detection. We represented objects in terms of parts composed of contours corresponding to object boundaries and symmetry axes; these are in turn related to edge and ridge features that are extracted from the image. We proposed a coarse-to-fine algorithm for efficient detection which exploits the hierarchical nature of the model. This led to a tractable framework to combine bottom-up and top-down computation. We learn our models from training images where only the bounding box of the object was provided. Furthermore, we automated the decomposition of an object category into parts and contours, and discriminatively learned the cost function that drove the matching of the object to the image using Multiple Instance Learning.
  The idea of using machine learning techniques for boundary detection was also considered in [23] where a novel approach for the segmentation of curvilinear structures in low signal to noise ratio images was introduced. The proposed method combined machine learning techniques, unsupervised clustering and linear programming. In particular, numerous invariant to position/rotation classifiers were combined to detect candidate pixels of curvilinear structure. These candidates were grouped into consistent geometric segments through the use of a state-of-the art unsupervised clustering algorithm. The complete curvilinear structure was obtained through an ordering of these segments using the elastica model in a linear programming framework. The same feature space was used as basis in [22] towards perceptual organization of part-based curvilinear structure representations towards their complete reconstruction that was able to deal with miss-detections through a local search algorithm.
  The problem was also considered in its temporal aspect [21] where a Markov Random Field formulation for the tracking of needles in fluoroscopic images was proposed using a single second-order MRF graph. Needles were represented by B-splines and each control point was associated with a random variable in a MAP-MRF formulation. In addition to the control points we introduced a single additional random variable representing the rigid transformation needles undergo during interventions. The incorporation of rigid transformations allowed recovering transformations even in the presence of large displacements which is not possible with existing MRF models for medical tool tracking.
- **Knowledge-based Segmentation with Geometric & Articulated-model Priors** Segmentation is a fundamental problem in medical image analysis. The use of prior knowledge is often considered to address the ill-posedness of the process. Such a process consists in bringing all training examples in the same reference pose, and then building statistics. During inference, pose parameters are usually estimated first, and then one seeks a compromise between data-attraction and model-fitness with the prior model. In [34], we introduced a novel higher-order Markov Random Field (MRF) model to encode pose-invariant priors and perform 3D segmentation of challenging data. The approach

encoded data support in the singleton terms that were obtained using machine learning methods, and prior constraints in the higher-order terms. A dual-decomposition-based inference method was used to recover the optimal solution. The segmentation of tissue classes of the human skeletal muscle was considered to demonstrate the potentials of the method.

In [24], we introduced a novel approach based on higher order energy functions which have the ability to encode global structural dependencies to infer articulated 3D spine models to CT volume data. The spinal column was modeled by a series of intervertebral transformations based on rotation and translation parameters. The shape transformation between the standing and lying poses was then achieved through a Markov Random Field optimization graph, where the unknown variables are the deformations applied to the intervertebral transformations. Singleton and pair wise potentials measured the support from the data and geometrical dependencies between neighboring vertebrae respectively, while higher order cliques were introduced to integrate global consistency. This framework was used as basis in [25] where a low-dimensional manifold embedding was created from a training set of prior mesh models to establish the patterns of global shape variations. Local appearance is captured from neighborhoods in the manifold once the overall representation converges. Inference with respect to the manifold and shape parameters is performed using a Markov Random Field (MRF). The optimization of the model parameters in both cases was achieved using efficient linear programming and duality. The resulting approach was geometrically intuitive, and led to excellent results on spinal column geometry estimation from CT data.

5.6. Model-based Segmentation & Deformable Image Fusion

Participants: Mickael Savinaud, Martin de la Gorce, Nikos Paragios.

The problem of model-based image fusion towards segmentation in small imaging studies was addressed in [30] where we presented a novel model-based approach to 3D animal tracking from monocular video which allows the quantification of bioluminescence signal on freely moving animals. The 3D animal pose and the illumination were dynamically estimated through minimization of an objective function with constraints on the bioluminescence signal position. Derived from an inverse problem formulation, the objective function enables explicit use of temporal continuity and shading information, while being able to handle important self-occlusions and time-varying illumination. In this model-based framework, we included a constraint on the 3D position of bioluminescence signal to enforce tracking of the biologically produced signal. The minimization is done efficiently using a quasi-Newton method, with a rigorous derivation of the objective function gradient. 3D accurate measurements with freely moving animal were obtained offering the possibility to study image biology at molecular scale in small animals with potentials applications in oncology or gene expression studies.

6. Contracts and Grants with Industry

6.1. Direct Industrial Collaborations

- GALEN has worked with Siemens towards the development of automatic segmentation tools for the human skeletal muscle [CIFRE Thesis: P-Y. Baudin].
- GALEN has worked with Intrasense towards the development of automatic segmentation tools for liver images as well as tumor detection [CIFRE Thesis: D. Pescia].
- GALEN has worked with Intrasense towards spatial position reasoning and understanding of low-grade gliomas brain tumors [CIFRE Thesis: S. Parisot, of 01/05/2010].
- GALEN has worked with BiospaceLab towards the development of automatic registration and fusion between fluoroscopic and video images towards signal enhancement [CIFRE Thesis: M. Savinaud, completed on 30/09/2010].
- GALEN has worked with GE-HealthCare towards development of automatic segmentation and tracking methods for assisting surgeons using interventional imaging [CIFRE Thesis: N. Honnorat].

- GALEN has worked with GE-HealthCare towards development of alternative CT reconstruction methods using compressed sensing and scarcity constraints [CIFRE Thesis: H. Langet].

6.2. Collaborative Industrial Projects

In the context of Medicen Paris Region competitive cluster, GALEN participates to the STEREOS+ [2009-2011] proposal that involves the École Nationale Supérieure d'Arts et Métiers as as second academic partner, four hospitals of Assistance publique - Hôpitaux de Paris (AP-HP), and two industrial partners, IOS-Imaging and Global-Imaging. The aim of the proposal is to build the next-generation orthopedic software work-station through the exploitation of low-dose X-Ray imaging.

7. Other Grants and Activities

7.1. Regional Initiatives

In the context of C3S, Carnot Institute Centrale Supélec Systems Sciences GALEN collaborated with the*Département Signaux & Systèmes Électroniques* of Supelec within:

- the DTI-Muscle project that aimed at developing medical-image based techniques for understanding neuro-muscular diseases through the processing of diffusion tensor images,
- the CT-based compressed sensing reconstruction project along General Electric Healthcare towards novel and efficient reconstruction methods that explore sparsity.

7.2. European Initiatives

- GALEN was recipient of five-year ERC-Starting/Consolidator DIOCLES: Discrete bIOimaging perCeption for Longitudinal Organ modElling and computEr-aided diagnosis grant that aims to:
  - Introduce a novel biomedical image perception framework for clinical use in disease screening and drug evaluation.
  - Leverage progress made in the field of machine learning, along with the novel, efficient, compact representation of clinical bio-markers, for computer aided diagnosis.
  - use emerging multi-dimensional signals, to perform longitudinal modeling and enhance our understanding of the effects of aging on a number of organs and diseases that do not present pre-disease indicators, such as neurological diseases of the brain, muscular diseases, certain forms of cancer, etc.
- GALEN has an established collaboration with the Chair for Computer Aided Medical Procedures and Augmented Reality at the Technical University of Munich, Germany in the area of image segmentation and deformable fusion [19], [33], [21], [36], [14]. Within this collaborative effort, F. Michel - PhD Candidate at GALEN - spent two months visiting the Chair for Computer Aided Medical Procedures and Augmented Reality at the Technical University of Munich (1/6/2010-1/8/2010).
- GALEN has an established collaboration with the Department of Computer Science at the University of Crete, Greece in the area of discrete optimization in biomedical imaging [16], [14], [19], [36], [32]. N. Komodakis is affiliated member of the GALEN group.

7.3. International Initiatives

- GALEN has an established collaboration with Department of Diagnostic Radiology of the University of Pennsylvania (UPenn) [18], [33], [29] in the area of deformable image fusion. Within this collaborative effort, Y. Ou - PhD Candidate at UPenn - spent two months visiting the GALEN group (15/4/2010-15/6/2010). Furthermore, N. Paragios has participated to National Institute of Health (NIH) grant proposals being submitted from Upenn.

- GALEN has an established collaboration with Department of Computer Science of the State University of New York at Stony Brook in the area of graph-matching [35] and understanding correlations between imaging and gne expressions data. Within this collaborative effort, K. Gkirtzou - PhD Candidate at GALEN - spent two weeks visiting the Bookheaven National Laboratory at Stony Brook (1/12/2010-15/12/2010).
- GALEN has an established collaboration with Department of Biomedical Engineering at Yale University in the area of tracking curvilinear structures. Within this collaborative effort, N. Honnorat - PhD Candidate at GALEN - spent two weeks visiting Yale (15/6/2010-15/8/2010).

8. Dissemination

8.1. Animation of the scientific community

8.1.1. Journal & Conference Editorial Activities

Participants: Nicolas Honnorat, Aristeidis Sotiras, Chaohui Wang, Iasonas Kokkinos, Nikos Paragios.

- **Editorial Boards**: N. Paragios is member of the editorial boards of the
  - Medical Image Analysis Journal (MedIA),
  - IEEE Transactions on Pattern Analysis and Machine Intelligence (T-PAMI),
  - International Journal of Computer Vision (IJCV),
  - Computer Vision and Image Understanding Journal (CVIU),
  - Journal of Mathematical Imaging and Vision (JMIV),
  - Image and Vision Computing Journal,
  - SIAM Journal in Imaging Sciences.

  N. Paragios is/was guest editor for (i) the Inverse Problems and Imaging Journal for the special issue in medical imaging, (ii) the Computer Vision and Image Understanding Journal for the issue in optimization for Vision, Graphics and Medical Imaging: Theory and Applications, (iii) the International Journal of Computer Vision for the issue dedicated to the 2010 edition of the European Conference in Computer Vision (ECCV'10).
- **Conference Boards**: N. Paragios was one of the program chairs of the European conference in Computer Vision (ECCV'10), and area chair for the Asian Conference in Vision (ACCV'10) and the IARP International Conference in Pattern Recognition (ICPR'10).
- **Conference Committees & Journal Reviewing Activities**:
  - N. Honnorat was reviewer for the Medical Image Analysis (MeDIA).
  - I. Kokkinos was reviewer for the International Journal of Computer Vision (IJCV), IEEE Transactions on Pattern Analysis and Machine Intelligence (IEEE T-PAMI), IEEE Transactions on Image Processing (IEE-IP), IEEE Transactions on Neural Networks and Image and Vision Computing (IVC).

    I. Kokkinos was member of the conference committee for the European Conference on Computer Vision (ECCV'10), IEEE Conference on Computer Vision and Pattern Recognition (CVPR'10), IEEE Workshop on Perceptual Organization in Computer Vision, Asian Conference on Computer Vision (ACCV'10), the International Symposium on Visual Computing (ISVC'10), the Indian Conference on Vision, Graphics and Image Processing.
  - N. Paragios was member of the conference committee for the Medical Image Computing and Computer Assisted Intervention (MICCAI'10), the IEEE Conference in Computer Vision (CVPR'10), the IEEE International Symposium on Biomedical Imaging (ISBI'10), the International Symposium on Visual Computing (ISVC'10), the IEEE Non-Rigid Shape Analysis and Deformable Image Alignment (NORDIA'10),

N. Paragios was reviewer for the Austrian Science Foundation, the European Union Commission (FP7), and the Agence National de la Recherche (ANR), the Austrian Science Foundation and the Swiss Research Council.

- A. Sotitas was reviewer for the IEEE Transactions on Medical Imaging (IEEE T-MI).
- C. Wang was reviewer for the Image and Vision Computing (IVC) and the IEEE Transactions on Biomedical Engineering (IEEE T-BE).

  C. Wang was member of the conference committee for the European Conference on Computer Vision (ECCV'10) and the International Conference in Pattern Recognition (ICPR'10).

8.1.2. Thesis & Doctoral Committees Participation

Participant: Nikos Paragios.

- **Reviewer of PhD Thesis Committees**: I. Kokkinos was reviewer for: (1) Anastasios Roussos - National Technical University of Athens.
- **Reviewer of PhD Thesis Committees**: N. Paragios was reviewer for: (1) Aditya Tatu - University of Copenhagen, (2) Yangming Ou - University of Pennsylvania.
- **Membder of PhD Thesis Committees**: N. Paragios was member for: (1) Charlotte Ghys - Ecole de Ponts, (2) Radhouene Neji - Ecole Centrale, (3) Salma Essafi - Ecole Centrale, (4) Ahmed Besbes - Ecole Centrale, (5) Regis Behmo - Ecole Centrale, (6) Mickael Savinaud - Ecole Centrale, (7) Ramya Narasimha, University of Grenoble.

8.1.3. Invited Lectures & Honors, Distinctions

Participants: Fabrice Michel, Aristeidis Sotiras, Iasonas Kokkinos, Nikos Paragios.

- **Distinctions/Honors**:
  - A. Sotiras was the recipient of the best student paper award of the IEEE International Symposium on Biomedical Imaging.
  - N. Paragios has received an ERC-Starting grant at the level of consolidator, was elevated to IEEE Fellow and participated to EU-US Frontiers of Engineering Symposium.
- **Tutorials**:

  I. Kokkinos was the organizer and chair of the Area Chair Colloquium of European Conference on Computer Vision (Paris'2010).

  N. Paragios was one of the organizers of the Intensity-Based Deformable Registration tutorial at the Medical Image Computing and Computer Assisted Intervetion (MICCAI'10).
- **Invited Presentations**:
  - F. Michel gave invited presentations at: Chair for Computer Aided Medical Procedures and Augmented Reality at the Technical University of Munich.
  - I. Kokkinos gave invited presentations at: Computer Vision and Image Science Group Seminar, University of California at Los Angeles.
  - N. Paragios gave invited presentations at: the International Workshop on Computer Vision, the Digiteo Scientific forum, the Computer Science Department of the University of California at Los Angeles.

8.2. Teaching

Participants: Nikos Paragios, Iasonas Kokkinos.

- **In Charge**: N. Paragios is in charge of the option Medical Imaging, Machine Learning and Computer Vision at the Department of Applied Mathematics of Ecole Centrale de Paris. This option consists of 6 classes in the above mentioned fields, 180 hours of teaching and is associated with the M.Sc. program of the ENS-Cachan in Applied Mathematics, Machine Learning and Computer Vision.
- **Instructor**:
  - I. Kokkinos was the instructor or has participated in:
    - Signal Processing Class (second year) at the Ecole Centrale de Paris (36 hours),
    - Introduction to Pattern Recognition (M.Sc. level) at the Ecole Centrale de Paris (24 hours),
    - Introduction to Computer Vision (second year) at the Ecole Centrale de Paris (36 hours).
  - N. Paragios was the instructor or has participated in:
    - Algorithmic Computer Vision Class (M.Sc. level) at the Ecole Normale Superieur (12 hours),
    - Advanced Mathematical Methods in Computer Vision (M.Sc. level) at the Ecole Normale Superieur/Ecole Centrale de Paris (24hours).

9. Bibliography

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