First Results and Future Developments of the MIBISOC Project in the IBISlab of the University of Parma

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ABSTRACT
“Medical Imaging using Bio-Inspired and Soft Computing” (MIBISOC) is a Marie Curie Initial Training Network (ITN) within the EU Seventh Framework Programme.

MIBISOC is a training programme in which sixteen Early-Stage Researchers (ESRs) are exposed to a wide variety of Soft Computing (SC) and Bio-Inspired Computing (BC) techniques, and face the challenge of applying them to the different situations and problems which characterize medical image processing tasks. Hence, the main goal of the project is to generate new methods and solutions from the combination of the ideas of experts from the area of Medical Imaging (MI) with those working on BC and SC applications.

The Intelligent Bio-Inspired Systems laboratory (IBISlab) in the University of Parma is one of the partners of this ITN. In this paper, we describe the work which is being developed in the IBISlab, as well as its future developments and main objectives, within the framework of this ITN.

Categories and Subject Descriptors
A.1 [Introductory and Survey]; J.3 [Life and Medical Sciences]

General Terms
Algorithms, Documentation, Experimentation

Keywords
MIBISOC, Intelligent Bio-Inspired Systems, Medical Imaging, Metaheuristics, General-purpose GPU computing, Object Detection, Object Tracking, Image Segmentation, Image Registration

1. INTRODUCTION
“MIBISOC: Medical Imaging Using Bio-inspired and Soft Computing” [15] is a Marie Curie Initial Training Network (ITN) funded by the European Commission within the Seventh Framework Program (FP7 PEOPLE-ITN-2008). The main goal of the network is to incorporate sixteen Early Stage Researchers (ESRs), enrolled in the programme after a selection among about 100 candidates, into eight leading research groups for thirty-six months under the umbrella of a formation program in Medical Imaging (MI) using Bio-Inspired Computing (BC) and Soft Computing (SC) which will allow them to obtain their PhD degree. The ESRs learn about a number of important MI-related problems, as well as about tested and emerging BC and SC techniques, and how to develop methods to solve the former problems by means of the latter techniques. In addition, they are exposed to other complementary topics such as project management, industrial property, ethical issues in research, negotiation techniques, etc., by means of the participation in a strictly coordinated international team activity.

As anticipated, the general area of this project deals with the application of intelligent systems, constituted by BC and SC techniques, to real-world MI applications. MI is at the heart of many of today’s improved diagnostic and therapeutic technologies, in which computer-based solutions offer the opportunity to obtain quantitative measurement of the medical condition, as well as the pre-processing techniques of filtering, sharpening, and focusing image details, to improve their interpretation by physicians. BC and SC have been successfully applied to each of the fundamental steps of medical image processing and analysis (e.g. restoration, segmentation, registration or tracking, see Figure 1). The natural partnership of humans and intelligent systems and machines in MI is expected to provide clinicians with tools which help them to take better decisions regarding diagnosis and treatment. MIBISOC aims to surpass the state-of-the-
Figure 1: MIBISOC partnership [15].

art approaches by applying intelligent systems constituted by SC-BC techniques to real-world MI applications.

The consortium is composed of world-wide recognized researchers from eight scientific institutions (six Universities, a R&D centre and an enterprise) that are involved as full partners, and four technical partners (a hospital, an enterprise, a Medical Company and a R&D centre) that provide relevant industrial and medical experience to the ESRs (see Figure 1). The collaboration of experts from the area of MI with those working on BC and SC applications to computer vision aims at generating new and viable methods and solutions from the combined ideas of the two communities.

The methodology that is followed has both a theoretical and a practical nature. Even though in most cases doctoral studies involve training for research, in MIBISOC we would like to focus on training by research. In this way, the outstanding research expertise of the partners in their respective areas, the practical know-how and the “hands on” scenarios provided by the industrial partners (companies and hospitals), supported by the experience of all the network participants and associated partners in organizational activities allow the network to implement a high-quality training program which favors the exchange of knowledge between the ESRs.

With this aim, a personalized, exhaustive and complementary career development plan (PCDP) has been designed for each of the ESRs, consisting of: i) a personalized research plan based on individual research projects; ii) local and network-wide specific training courses, both in face-to-face and virtual modalities; iii) the network’s complementary skills courses, workshops and final conference; and iv) research visits to the different international partners.

The Intelligent Bio-Inspired Systems laboratory (IBISlab) of the University of Parma (UPARma in Figure 1) is one of MIBISOC’s nodes, and is mainly investigating evolutionary and swarm intelligence-based approaches to image analysis such as:

- novel approaches to medical image analysis fully based on bio-inspired algorithms, or in which bio-inspired algorithms are an essential part [5];
- techniques for detecting anatomical districts of interest or recognizing body postures, to be used in tasks like: matching of real images with anatomical atlases, extraction of features of clinical/physiological interest, 3D reconstruction and visualization, detection of morphological or structural anomalies, and human body pose estimation and tracking.

For further information about the MIBISOC project, the interested reader is kindly asked to refer to Section 4.2 in [9] or to visit [15].

2. BACKGROUND

This section briefly introduces some of the fundamental computer vision and soft computing techniques applied to medical image processing in the IBISlab, within a wider research framework in which model-based detection and recognition techniques are studied and developed.

2.1 Model-based object detection and recognition

Many object detection tasks, like the localization and segmentation of anatomical structures, can be reformulated as global optimization problems. In this optimization process, a metaheuristic is used to find the best parameters of an object model or deformable template, which directly encode both the object’s position and appearance within an image by means of a specific transformation which maps model coordinates to coordinates of the image plane. Most applications currently under development in the IBISlab can be framed within a common general approach. In this approach, a function, which represents the similarity between object models and an image region, is to be maximized.

Different metaheuristics are being used and compared to tackle problems of medical and industrial interest. In the last two decades, research on global optimization has been very active, and many different deterministic and stochastic algorithms for continuous optimization have been developed. Among the stochastic approaches, Swarm Intelligence (SI), based on animal social group behavior, and Evolutionary Computation (EC) [14], inspired by the natural process of Darwinian evolution, have a number of features that make them attractive: implicit parallelism, robust and reliable performance, global search capability, no need of specific information about the problem to solve, easy implementation, good insensitivity to noise, and no requirement for a differentiable or continuous objective function. Among these techniques, Differential Evolution (DE) [40] and Particle Swarm Optimization (PSO) [27] are among those who have recently been most successful [10, 37].

Giving for granted that most readers are well acquainted with EC and SI techniques, before describing the most relevant medical applications we are developing, in the following of this section we describe only very shortly the three population-based optimization techniques on which most of our research is based, while we give some more detailed, albeit basic, information about deformable models and GPU
computing, which are two of the most characterizing "ingredients" of our work.

2.2 Particle Swarm Optimization

PSO is a bio-inspired optimization algorithm based on the simulation of the social behavior of bird flocks. In the last fifteen years PSO has been applied to a very large variety of problems and numerous variants of the algorithm have been presented.

During the execution of PSO a set of particles moves within a (fitness) function domain searching for its optimum (best fitness value). The motion of each particle is driven by the best positions visited so far by itself and by the entire swarm (ghost PSO) or by some pre-defined neighborhood of the particle (lbest PSO). Consequently, each particle relies both on "individual" and on "swarm" intelligence, and its motion can be described by the following two simple equations which update the particles’ position and velocity:

\[ P_n(t) = P_n(t-1) + v_n(t) \]

\[ v_n(t) = \omega \cdot v_n(t-1) + c_1 \cdot \text{rand}() \cdot (P_{\text{lbest},n}(t-1)) + c_2 \cdot \text{rand}() \cdot (B_{\text{lbest},n}(t-1)) \]

where \( P_n(t) \) and \( v_n(t) \) are the position and velocity of the \( n \)th particle in iteration \( t \); \( c_1, c_2 \) and \( \omega \) (inertia factor) are positive constants, \( \text{rand}() \) returns random values uniformly distributed in \([0,1]\), \( BP_n \) is the best-fitness position visited so far by the particle and \( B_{\text{lbest},n} \) is the best-fitness position visited so far by any particle of a neighborhood which may be as large as the current swarm: in this case, this position corresponds to the global best.

In particular, in our implementations of PSO, several alternatives have been tested, from a linearly decreasing inertia factor, to an inertia factor whose value is adapted to the fitness function of each particle, and different kind of swarm topologies in lbest PSO.

2.3 Differential Evolution

DE, first introduced by Storn and Price [40], has recently been shown to be one of the most succesful Evolutionary Algorithms (EAs) applied to global continuous optimization [10]. Unlike traditional EAs, DE perturbs the current population members with the scaled differences of randomly selected and distinct individuals. In the first iterations, the elements are widely scattered in the search space and have great exploration ability while, as optimization proceeds, the individuals tend to concentrate in the regions of the search space with better values, so the search automatically focuses on the most promising areas. In DE, every element acts as a parent vector and, for each of them, a donor vector is created. In the original version of DE, the donor vector for the \( z \)th parent \( X_z \) is generated by combining three random and distinct elements \( X_{r_1}, X_{r_2} \) and \( X_{r_3} \). The donor vector \( V_i \) is calculated as follows:

\[ V_i = X_{r_1} + F \cdot (X_{r_2} - X_{r_3}) \]

where \( F \) (scale factor) is a parameter that strongly influences DE’s performances and typically lies in the interval \([0.4, 1]\). After mutation, every parent-donor couple generates an offspring (the so-called trial vector) by means of a crossover operation. Two kinds of crossover are typically used: binomial (also called uniform) and exponential. Besides \( F \), the crossover rate \( C_r \) is another parameter which regulates the searching behavior of DE.

2.4 Scatter Search

Scatter Search (SS), originally proposed by Glover [19], is based on a systematic combination between solutions, instead of a randomized one, as usually happens in EAs, taken from a considerably reduced evolved subset of solutions named the reference set (usually between five and ten times smaller than typical EA population sizes). SS is composed of 5 structural “blocks” or methods:

1. Diversification Generation: a population of solutions \( P \) is generated with a certain degree of quality and diversity. The reference set \( R \) is then drawn from \( P \), and it is composed of the \(|R_1| \) solutions with best fitness, and the \(|R_2| \) solutions from \(|P|\) with the maximum euclidean distance to the reference set (hence, \(|R| = |R_1| + |R_2|\)). The evolution process will work only over \( R \);

2. Solution Recombination: in most problems a specific solution recombination method is needed, which can be selectively applied (for example, only to the best solutions) and/or choosing random elements. In many cases an existing genetic algorithm crossover operator can be employed (like in many of our implementations where the BLX-\( \alpha \) is used);

3. Subset Generation: the procedure generates, in a deterministic way, subsets of \( R \) to which the recombination method is applied.

4. Improvement: to obtain high-quality solutions, an improvement method is applied to original solutions and/or combined solutions (usually a “local search”, like Solis&Wets, Luus-Jaakola, Random Search or Simulated Annealing that, among others, were tested in our experiments);

5. Reference Set Update: once a new solution is obtained (applying the combination method) it replaces the worst solution in \( R \) only if this improves the quality of the reference set in terms of fitness and/or diversity.

2.5 Deformable Models

The term “deformable models” was first used in the late eighties [41] with reference to curves or surfaces, defined within the image domain, that are deformed under the influence of “internal” forces, related with the curve features, and “external” forces, related with the image regions surrounding the curve. Internal forces enforce regularity constraints and keep the model smooth during deformation, while external forces are defined such that the model is attracted toward an object or other features of interest within the image. One of the first examples, called “snakes” or Active Contour Models, was presented by Kass [26].

Active Shape Models (ASMs) [8] add more prior knowledge to deformable models. These shape models derive a “point distribution model” from sets of labelled points (landmarks) selected by an expert in a training set of images; in each image, a point, or set of points, is placed on the object corresponding to its label. The model considers average positions of such points and the main modes of variation found in the training set. While this kind of model has problems with unexpected shapes, since an instance of the model can
only take into account deformations which appear in the training set, it is robust with respect to noise and image artefacts, like missing or damaged parts. Active Appearance Models [7] extend ASMs by considering not only the shape of the model, but also other image properties, like intensity or color.

Deformable templates are a kind of deformable models that represent shapes as deformations of a given prototype or template. They have been successfully applied to object tracking [45] and object matching [24]. To define a deformable template, one needs, firstly, to mathematically define a prototype which describes the prior knowledge about the object shape as the most likely appearance of the object being sought. Secondly, one needs to provide a mathematical description of the possible relationships between the template and all object shapes which can be obtained by applying admissible transformations which can deform the basic template and turn it into the target object, as appears in the image. These templates are specified by a set of parameters that defines the possible variations of the target class of objects. By modifying these parameters, it is possible to deform the template until it becomes most similar to the target.

Although originally developed for computer vision applications to natural scenes and computer graphics problems, the potential of deformable models in medical image analysis has already been proven [22, 23].

2.6 General-purpose GPU computing

Modern graphics hardware has gained an important role in the area of parallel computing. Graphic cards have been used in 3D graphics applications and gaming but, recently, they have also been used to accelerate general-purpose computation. This is usually referred to as “General-Purpose Graphics Processing Unit (GPGPU) programming”.

CUDA™ (Compute Unified Distributed Architecture) is a parallel computing environment by nVIDIA™ which exploits the massively parallel computation capabilities of its most recent GPUs (containing up to several hundreds of execution cores that can perform the same operations on different data). The programming model of CUDA™ requires that the problem under consideration be partitioned into many independent sub-tasks (thread blocks), performed in parallel by a number of cooperating threads. In particular, the nVIDIA CUDA-C is an extension of C language that allows development of GPUs routines (kernels), that may be executed in parallel by N different CUDA™ threads, following the Single Instruction Multiple Thread (SIMT) model [34]. Therefore, CUDA™ is a programming model and instruction set architecture that leverages the parallel computing capabilities of nVIDIA™ GPUs to solve complex problems more efficiently than a CPU.

EC and SI algorithms, like most population-based optimization methods, are inherently parallel, so implementing them in parallel seems to be the way to make practical use of these powerful search and optimization tools. In the IBIS-lab our attention has been mainly focused on the parallel implementation of PSO, DE and SS.

The first parallel versions of PSO, less than one decade ago, relied on multiprocessor parallel machines or cluster computing systems. With the introduction of GPUs, research shifted towards parallel PSO on the GPU to alleviate multi-processor and cluster systems inefficiencies, such as network overhead, shared memory access, etc. In 2009 and 2010, respectively, the first implementations of PSO and DE based on nVIDIA CUDA™ were developed [11, 12], showing clear advantages of the GPU-based implementation, in terms of computation efficiency, with respect to the corresponding sequential code. Also in 2009, a hybrid between GPU-based PSO and pattern search was developed to enhance the convergence of PSO [46]. More recently, other implementations of DE have been developed [29], and fast versions of PSO have been implemented by relaxing the synchronicity constraints between particles [32].

3. ONGOING PROJECTS

3.1 Segmentation of Anatomical Brain Structures in Biomedical Images

Among the large number of applications of automatic localization and segmentation methods in clinical and experimental medicine, there is great interest in automated methods to accurately, robustly, and reproducibly localize the hippocampus in brain images, after discoveries which established its role as an early biomarker for Alzheimer’s disease and epilepsy [3].

We consider the problem of extracting the region where the hippocampus is located from the mouse brain images included in the Allen Brain Atlas (ABA), a huge, publicly available image database, which has recently provided scientists with a gene-expression map for future study and investigation. The ABA contains a genome-scale collection of histological images (cellular resolution gene-expression profiles) obtained by In Situ Hybridization (ISH) of serial sections [1] of mouse brains.

The fully automatic 2D localization method we propose [42] relies on atlas-based registration (the selection of the reference slice in the atlas corresponding to the image under consideration, using a two-step affine transformation) and the optimization of the parameters of a parametric deformable model inspired by ASMs. We search the hippocampus region as the region which minimizes a fitness function measuring the distance between the hypothesized position of the model and the image; to do so we use a stochastic global search to...
deal with the multi-modality of the function we want to minimize (see Figure 2).

We first approached the problem using PSO, comparing later the results obtained by other optimization techniques, like Simulated Annealing (SA) [28], Genetic Algorithms (GA) [20], SS and DE, finding that this last method outperformed the other four in this task.

It is important to notice that the use of DE in association with deformable models for medical image analysis is quite new. In fact, we are only aware of another paper [33] which deals with such a topic.

The points located in this stage are then used as seeds for the segmentation phase. We compared two segmentation methods. The first combines an iterative thresholding technique based on Otsu’s method [36] and a region-growing technique that relies on Random Forests [4]. The second technique is based on the Level Set [35] method. This results in a novel hybrid combination of parametric and geometric deformable models, where the former are used to initialize the latter.

To test the performance of the method, a ground truth was created by manually segmenting the hippocampus in 30 real images. In order to avoid erroneous or incomplete manual segmentations, these were supervised by an expert in molecular biology. Every image was manually segmented five times and, for each group of five manual segmentations, the intersection and union images were calculated. Also 30 synthetic images were drawn including small and big ellipses, which simulate cells, and adding gaussian and salt and pepper noise. The performance was evaluated in terms of True Positives, False Positives, Dice Similarity Coefficient and Hausdorff Distance. Both methods achieved an accuracy close to 91% on the test set of 30 synthetic images, whilst, on real images, the first method achieved better results with an average accuracy of 89.65% using the consensus image (which contains the pixels segmented in at least three out of five manual segmentations) as ground truth.

The main characteristics of the method we developed can therefore be summarized as follows:

- General approach. We have divided our method in: i. initialization of the deformable model; ii. robust localization of the structure of interest (Figure 3); and iii. segmentation. A different technique can be applied for every image modality or subcortical structure in these three phases; in fact, we have divided the processing pipeline into these three stages to keep them independent from one another. The generality of the system is also associated to the simplicity of the models we use, which include the minimum possible problem-specific information.

- Use of basic prior knowledge: the most invariant feature of the hippocampus is its shape. This can be deformed according to statistical patterns dependent on the brain section represented in the target image, which can be determined by comparing the original image with the atlas. Besides this, the hippocampus substructures we want to locate are usually darker than the immediately surrounding regions.

- General applicability: the method is applicable to virtually all cases in which one can rely on a reference atlas. A parametric model can be associated to each reference image in the atlas, and the localization of the anatomical structure under investigation can be turned into an optimization problem. In order to refine the segmentation, a classifier trained with patterns from the structure of interest can also be useful. In this stage, we tried several Ensemble Classifiers, like Random Forests, to improve segmentation accuracy.

3.2 Human Body Pose Estimation in Video Sequences

Three-dimensional human body pose estimation from video is the problem of extracting an accurate estimation of the posture of a human body, along with its location in space, from an image or a frame within a video stream. The techniques that deal with this problem have many potential applications in animation, interactive games, motion analysis (sports, medical) and surveillance. In particular, using gestures for interaction with computer-assisted systems can be of great benefit, particularly in scenarios where traditional input devices are impractical, such as the medical operating room [39]. Another interesting application can be found in elderly people healthcare. For instance, for an elderly person a fall can result in quite serious injuries because of his/her fragile bone structure. Therefore, fall detection (which usually implies object tracking and movement classification) would be a possible utilization of this kind of techniques [38, 47]. Furthermore, robust and accurate object tracking algorithms could be also applied in other contexts, like tracking and detection of anatomical structures and abnormalities.

Human body pose estimation is a complex task that has been invariably formulated as a high-dimensional search problem, due to the complexity of the human body pose parame-
terization. It has been tackled by trying to reduce the complexity of the search while also relying on effective search schemes. The search complexity can be reduced based on local predictions, e.g., using particle filters [2, 13], or by partitioning the search space into smaller, more manageable subspaces [2]. The use of machine learning techniques to define specific motion models for particular actions from training data collected in advance has also been considered [6, 43]. These approaches suffer from various setbacks. The particle-filtering solutions critically rely on a high number of particles to adequately represent the posterior distribution, which in turn increases their computational complexity beyond practical use when considering a wide variety of motion. As well, relying on pre-trained motion models causes the human body tracking approaches to lose their generalisation abilities, which points to methods which can reliably provide motion estimates without a pre-trained motion model [18].

In [25], an effective search algorithm was proposed, which is capable of recovering the pose without any prior knowledge of the nature of motion. The main drawback of the method is its huge computational complexity, which makes the time required for execution of a standard sequential implementation hardly acceptable. However, relying on the parallel nature of both the search algorithm and the multi-view pose estimation problem by implementing the approach on a GPU, we showed that we could reach execution times acceptable for practical purposes [31] (see some results in Figure 4).

Again, to solve this task, a model-based approach is used. In this case the body model consists of two layers, the skeleton and the skin. The skeleton layer is defined as a set of homogeneous transformation matrices which encode the information about the position and orientation of every joint with respect to its parent joint in the kinematic tree hierarchy. The matching function compares the silhouettes generated by the model in its candidate pose, with the silhouettes extracted from the original images. In Figure 5, one can see how this process iteratively tries to improve a candidate solution, a model deformed in some way, with regard to a given measure of quality (the overlapping of the model with the original image). So, the search for the best model transformation is driven by the similarity function and the metaheuristic used to optimize it. In each iteration, the model is deformed and superimposed to the original image, in order to compute the degree of overlapping with the target image, which determines the fitness value. The search is over when a stopping criterion is met.

DE and PSO were used for the optimization process, but other techniques, which take time into consideration, can be even more useful and be applied in future implementations: Hierarchical Temporal Memory (HTM) [21], temporal Self Organizing Map [44], or bio-inspired hierarchical classifiers, like the Neocognitron [17].

### 3.3 International and multidisciplinary collaboration

The EU Framework Programmes for Research and Technological Development promote funding programmes created to support and encourage research in the European Research Area. One of the main objectives is to stimulate collaboration among European research institutions. The PCDP defined for each ESR in MIBISO (see Section 1) includes several collaborations between partners, and at least two research stays/secondments at other network partners. The network promotes the co-supervision of the ESRs’ research training projects and PhD studies. The additional co-supervision from another participant or associated partners would enrich the multidisciplinary and intersectoral aspects of the research carried out by the ESRs and would enhance the collaboration between the network partners.

MIBISO has given the IBIS laboratory the opportunity to establish collaborations with various partners of this European network. In particular, we have relied on the support of members of the School of Computer Science of the University of Nottingham (United Kingdom), experts in the application of geometric deformable models to MRI brain image segmentation [16], in implementing and the Level Set method and applying it to the segmentation of the hippocampus in histological images. As well, we are collaborating with the IRIDIA in the Université Libre de Bruxelles (Belgium) on the automatic parameter configuration [30] of the different GPU implementations of metaheuristics, that were compared in terms of efficiency, parallelism and execution time.

Other possible collaborations which we are presently considering involve the Universitätsklinikum Freiburg (Germany), the European Center for Soft Computing in Mieres (Spain) and the Signal and Image Processing for Neuroscience group.
of the Centre National de la Recherche Scientifique in Paris (France).

4. CONCLUSIONS AND FUTURE DEVELOPMENTS

One of the main motivations for this network is the decisive bet of EU on research and on the consolidation of a knowledge-based society. A network with these features favors professional interaction and mutual enrichment, at the scientific and intellectual level, thanks to its multidisciplinary nature. This network shows the need for collaboration in various fields (from medicine and biology to artificial intelligence, statistics and image processing) to achieve the excellence in a vital field for the citizenship welfare, like health-care.

Among the future developments for our lab, as well as for MIBISOC, the following items could be mentioned:

- Publications of high impact factor that materialize the investigations made to date, where new and better solutions in the medical image processing field are provided (in terms of computational resources, simplicity and understandability of the solutions, or execution speed).

- Software tools designed for the mentioned areas (processing, analysis and computer vision techniques applied to medical imaging using bio-inspired and soft computing).

- Strengthening of this collaborative, multidisciplinary, and international network by further research stays and collaborations, as has been done so far.

With regard to the IBIS lab activities, as regards the project related to the automatic localization of subcortical structures in the brain, we aim to study and compare the results of the application of other approaches, ranging from the use of probabilistic maps to fuzzy logic, and of other kinds of deformable models and representations. Also, we would like to test the system with other kinds of image modalities like MRI.

As regards the human body pose estimation project, advanced techniques that take time into consideration will be used, like HTM or temporal SOM, to be able to recognize, and possibly assess, human actions. A very useful and interesting approach would be the comparison between these techniques and their combination with hardware economically accessible to users, like Microsoft Kinect™.

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6. REFERENCES


