Multimodal Medical Image Registration Using Particle Swarm Optimization: A Review

Leonardo Rundo[1,2], Andrea Tangherloni[1], Carmelo Militello[2], Maria Carla Gilardi[2,3], Giancarlo Mauri[1,3]
[1]Department of Informatics, Systems and Communication (DISCo), University of Milano-Bicocca, 20126 Milano, Italy
[2]Institute of Molecular Bioimaging and Physiology (IBFM), Italian National Research Council (CNR), 90015 Cefalù (PA), Italy
[3]SYSBIO - Centre of Systems Biology, 20126 Milano, Italy
{leonardo.rundo, andrea.tangherloni, mauri}@disco.unimib.it; {carmelo.militello, mariacarla.gilardi}@ibfm.cnr.it

***Abstract*— Intensity-based registration techniques have been increasingly used in multimodal image co-registration, which is a fundamental task in medical imaging, because it enables to integrate different images into a single representation such that complementary information can be easily accessed and fused. These schemes usually require the optimization of some similarity metric (e.g., Mutual Information) calculated on the input images. Local optimization methods often do not obtain good results, possibly leading to premature convergence to local optima, especially with non-smooth fitness functions. In these cases, we can adopt global optimization methods, and Swarm Intelligence techniques represent a very effective and efficient solution. This paper focuses on biomedical image registration using Particle Swarm Optimization (PSO). Several literature approaches are critically reviewed, by investigating modifications and hybridizations with Evolutionary Strategies. Since biomedical image registration represents a challenging clinical task, the experimental findings encourage further research studies in the near future.**

***Keywords*— Swarm Intelligence; Particle Swarm Optimization; Biomedical image registration; Multimodal medical imaging; Mutual information**

I. INTRODUCTION

Image co-registration is a fundamental task in medical imaging because it enables to integrate different images into a single representation (i.e., the same reference system), allowing physicians and researchers to access at this complementary information more easily and accurately [1][2]. Fused image data can improve medical diagnosis, surgery planning and simulation as well as intra-operative navigation. The choice of the modality depends strongly on the medical task. In radiotherapy planning, for instance, dose calculation is based on the Computed Tomography (CT) data, while tumor delineation is often better performed on the corresponding Magnetic Resonance Imaging (MRI) scans, especially in soft tissue imaging (e.g., brain or prostate) [3]. The same anatomical district of the human body is often imaged with different modalities (Fig. 1). In particular, morphologic images, which define the anatomy of organs or pathological tissues, can be integrated with functional ones, which describe the cellular physiology or the metabolism (Positron Emission Tomography, PET). These images are used in a complementary fashion to gain additional insights into biological phenomena and pathologies. Even though combining appropriately different modalities is definitely useful, multimodal images even concerning the same subject generally differ by local geometric differences. Therefore, in order to perform quantitative and precise evaluations on biomedical imaging data, such images have to be mapped into the same coordinate system by means of the alignment process, named *biomedical image co-registration*. Medical image registration algorithms can be conveniently applied in: *(i)* intra-modality matching, for patient follow-up (e.g., tumor response assessment over the time); *(ii)* inter-modality matching, for comparisons and quantitative measurements concerning images acquired with different modalities.

The aim of this work is to provide to the reader an overview on biomedical image registration using *Particle Swarm Optimization (PSO)*, which is a population-based stochastic optimization algorithm [4][5]. Notably, to the best of our knowledge, no other *Swarm Intelligence* techniques have been applied to this problem so far. The different approaches proposed in the literature are examined, by thoroughly investigating various modifications and hybridizations with evolutionary strategies and genetic algorithms. This manuscript is organized as follows: section II explains the theoretical background regarding medical image co-registration as well as the *PSO* technique; section III describes and reviews biomedical image registration approaches based on *PSO*; in section IV, the experimental findings obtained in the experiment trials by the different approaches are illustrated and discussed; some conclusive remarks are provided in section V.

II. THEORETICAL BACKGROUND

In this section, the theoretical framework underlying this study is presented. First, a detailed description of biomedical image registration is reported, with particular attention to intensity-based techniques. Afterwards, *Particle Swarm Optimization (PSO)* will be introduced.

A. Biomedical Image Registration

An image co-registration stage is mandatory to integrate and quantitatively compare biomedical imaging data originating from different modalities. As a matter of fact, image registration is able to bring the different medical datasets, concerning the same patient, into the same space. In this way, it will be possible to make quantitative and meaningful comparisons between the Regions of Interests (ROIs), such as organs and tumors, obtained by processing several image series from different scanners and modalities [6].

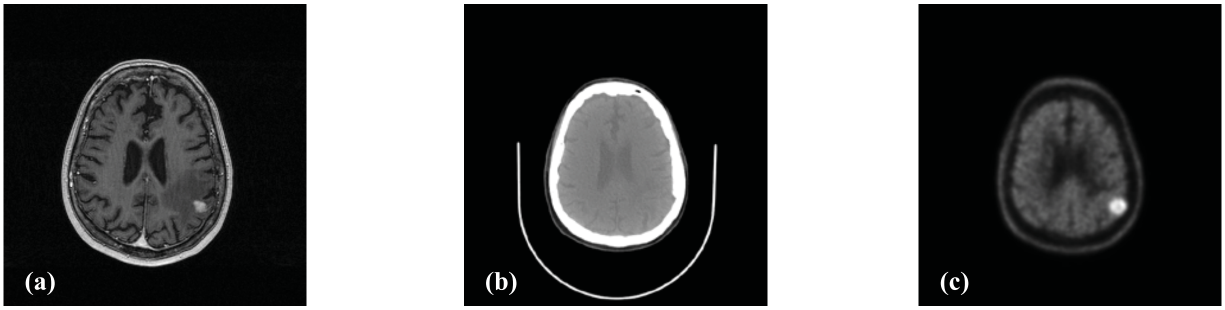

Fig. 1. Examples of different medical image modalities concerning the same subject affected by brain tumor: (a) Magnetic Resonance Imaging; (b) Computed Tomography; (c) Positron Emission Tomography.

Registration approaches can be principally distinguished in feature-based and intensity-based schemes [2]:

- *Feature-based techniques* find correspondences between geometrical image features (e.g., points, lines, contours, surfaces) or landmarks (external or anatomical). Either image features or landmarks are first extracted from the input images, and then a transformation is established according to the correspondence between the found features. However, segmenting and finding correspondences are very difficult tasks.
- *Intensity-based techniques* directly exploit image intensities to compute the transformation that maximizes a similarity metric by searching in a certain space of transformations and comparing intensity patterns. The main advantage of these schemes is that explicit image segmentation or feature extraction is not required.

This review is focused on intensity-based registration techniques, since they are the most suitable for applying *Swarm Intelligence* approaches. Fig. 2 shows the overall flow diagram of the biomedical image registration process, by using an intensity-based technique.

From an algorithmic perspective, image co-registration involves finding the parameters, i.e., a geometric transformation matrix $\mathbf{T}$, which either maximize or minimize some objective function, a.k.a. fitness function $f(\cdot)$. Therefore, image co-registration can be modeled as an iterative procedure by successive refinements. In each iteration, the current estimate of the transformation $\hat{\mathbf{T}}$ is used to calculate a similarity measure. Afterwards, the optimization algorithm makes another (hopefully better) estimate of the transformation, evaluates the similarity measure again and continues to iterate until the convergence condition is achieved (i.e., no transformation can improve the value of the similarity metric above a preset tolerance threshold ε or the number of possible iterations is achieved). The multimodal registration process starts from two images A and B probably characterized by different Fields of View (FOVs): A is used as source image (floating) while B is the reference image (target). The reference imaging modality is usually selected according to the higher spatial resolution and image content. For instance, in PET/MRI registration, MR images are chosen as target images because they convey more anatomical information than PET images.

The geometric transformation $\mathbf{T}$ is defined only in the region of overlap of the image FOVs, and must take into account image sampling and resolution. It is also important to note that the images are discrete. The discretization is determined by the sampling grids, which are different when FOVs are not the same [7]. Even if images A and B have exactly the same sampling grid, the grid points will not normally coincide in the volume of overlap and an interpolation step is therefore necessary. Realignment and reslicing operations are mandatory to get a one-to-one mapping between different modality slices. Especially, in iterative registration algorithms, an accurate interpolation method is required [3][6] (e.g., B-Spline interpolation).

In intensity-based registration techniques, the three core components are: *(i)* the search space (parameter space); *(ii)* the similarity metric (objective function); *(iii)* the search strategy (optimization algorithm).

1. Search Space

The search space Ω is the set of potential transformations used to align the images. Each point in the parameter space corresponds to a different estimate of the transformation. Accordingly, the parameter space can be thought as a high-dimensionality function in which the value of each location corresponds to the value of the similarity measure for that transformation estimate. Geometric transformations may be rigid, affine, and elastic.

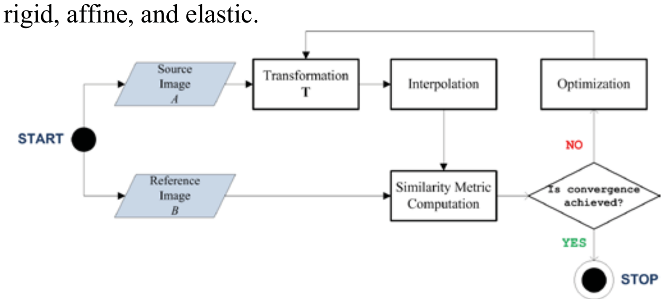

Fig. 2. Flow diagram of the biomedical image registration process, by using an intensity-based technique.

Three dimensional (3D) rigid-body registration has six degrees of freedom, regarding:

- translations along the three axes of the reference system x, y and z, denoted by the displacements t_x, t_y and t_z, respectively;
- rotations around the x, y and z axes, denoted by the angles α, β and γ, respectively.

In 3D rigid-body registration, the mapping of the coordinates $\mathbf{p}_A = (x\ y\ z)^{\mathrm{T}}$ into the transformed coordinates $\mathbf{p}'_A = (x'\ y'\ z')^{\mathrm{T}}$ can be suitably formulated as a matrix multiplication in homogeneous coordinates with the geometric transformation matrix $\mathbf{T}$.

Some registration algorithms increase the number of degrees of freedom by allowing for anisotropic scaling (giving nine degrees of freedom) and skews (giving twelve degrees of freedom). A transformation that includes scaling and shearing as well as the rigid-body parameters is referred to as affine, and has the important characteristics that it can be described in matrix form and that all points, straight lines and planes are preserved. Rigid-body registration is widely used in medical applications where the structures of interest are either bony or are enclosed in bones (e.g., head, neck, pelvis, leg or spine), but the errors are likely to be larger. The use of an affine transformation rather than a rigid-body one does not greatly increase the applicability of image registration, as there are not many organs that only stretch or shear. Tissues usually deform in more complicated ways. However, errors introduced by the scanner may occur, resulting in scaling or skew terms, and affine transformations are sometimes used to overcome these problems [7]. For most organs in the body, many more degrees of freedom are necessary to describe the tissue deformation with adequate accuracy, thus elastic or non-rigid methods are required to cope with local differences between the images.

However, for global elastic transformation, the number of parameters to be optimized is generally too large (often many thousands) to be feasible in practice. Therefore, two-step intensity-based registration approaches are used. In the first step, the global affine medical image registration is used to establish a one-to-one mapping between the two images to be registered. Afterwards, the images are registered up to small local elastic deformation.

2. *Similarity metric*

The similarity metric is an indicator that quantifies the degree of closeness between features or intensity values of two images. The Sum of Squared intensity Differences (SSD), correlation coefficient, ratio image uniformity are often utilized in intra-modality registration [7]. Because of the similarity of the intensities in the images being registered, these subtraction, correlation and ratio techniques are pretty intuitive. With inter-modality registration, the situation is quite different: there is, in general, no simple relationship between the intensities in the images A and B [6].

Mutual Information (MI) $I(A,B)$ is an information theoretic concept for estimating the degree of dependence of the random variables A and B, with marginal probability distributions $p_A(a)$ and $p_B(b)$, by measuring the distance between the joint distribution $p_{AB}(a,b)$ and the distribution associated to the case of complete statistical independence $p_A(a) \cdot p_B(b)$ [3][8]:

$$I(A,B) = \sum_{a,b} p_{AB}(a,b) \log \frac{p_{AB}(a,b)}{p_A(a) \cdot p_B(b)}. \tag{1}$$

Let the random variables A and B represent the image intensity values a and b concerning the pairs of voxels in the two images to be registered, respectively. Estimations for the joint distribution and the marginal distributions can be simply obtained by normalizing the joint and marginal histograms of the overlapping parts of both images. In general, the input images are also smoothed slightly, by means of their histogram. This makes the cost function (i.e., similarity metric) as smooth as possible to give faster convergence and less chance of being trapped in local minima.

The intensities a and b are related through the geometric transformation $\mathbf{T}$. The *MI* registration criterion states that the images A and B are geometrically aligned by the transformation $\mathbf{T}$ for which $I(A,B)$ is maximal. Therefore, the objective of intensity-based registration is to find an estimation of the transformation $\mathbf{T}$ that best aligns the source image A against the reference image B : $\hat{\mathbf{T}} = \arg\max_{\mathbf{T}\in\Omega} \{ I(\mathbf{T}(A), B) \}$.

The results presented by Maes *et al.* [3] proved that sub-voxel registration differences with respect to the stereotactic reference solution can be obtained for CT/MRI and PET/MRI matching without using any prior knowledge about the gray-value content of both images and the correspondence between them. As a matter of fact, *MI* is the most intensively investigated criterion for registration of intra-individual human brain images [1]. *Normalized Mutual Information (NMI)* is also frequently used as the cost function to be optimized [9]. Especially, when misalignment can be large with respect to the imaged FOVs, a criterion invariant to image overlap statistics should be used:

$$I_N(A,B) = \frac{H(A) + H(B)}{H(A,B)}. \tag{2}$$

where $H(\cdot)$ and $H(\cdot,\cdot)$ are the marginal and the joint entropies, respectively.

3. *Optimization of Similarity Metrics*

Intensity-based registration techniques determine the registration transformation $\mathbf{T}$ by optimizing a certain voxel similarity measure. Unfortunately, parameter spaces for image registration are frequently not so simple. There are often multiple optima within the parameter space, and the registration can fail if the optimization algorithm converges to the wrong optimum. Some of these optima may be very small, caused either by interpolation artifacts or a local good match between features or intensities [7]. As explained previously, these small optima can often be removed from the parameter space by smoothing the images before the registration.

Local methods, such as Powell's direction set method, Nelder-Mead simplex algorithm, conjugate gradient, Levenberg-Marquardt algorithm, are usually employed in image registration [10]. Because many similarity metrics (i.e., functions of transformation parameters) are generally irregular and rough, especially in multimodal image registration, local methods are more accurate when the initial orientation is very close to the transformation that yields the best registration [11]. These strategies are also susceptible to premature convergence to local optima, especially for non-smooth functions. An approach to address this issue is to apply multiresolution techniques, whereby images are aligned at increasing resolutions with initial orientations from the previous (lower) resolution registration result. However, these hierarchical methods frequently become trapped in local optima, as the global optimum may not be present in lower resolutions [7]. Global optimization is often required for dealing with the most general and tricky situations. Such global approaches include simulated annealing, tabu search, genetic algorithms and evolutionary strategies. Efficiency is the primary reason that local techniques are preferred for registration. Efficient global optimization may gain acceptance if a significant improvement in accuracy can be demonstrated.

For intensity-based registration, the problem is even more complicated. The desired optimum when registering images using voxel similarity measures is not often the global optimum, but it is one among the local optima [7]. A solution to this problem is to start the algorithm in the proximity of the correct optimum, which is within the portion of the parameter space in which the algorithm is more likely to converge to the correct optimum than the incorrect global one. In practical terms, this requires that the starting estimate of the registration transformation is reasonably close to the correct solution.

B. Particle Swarm Optimization

Swarm Intelligence (SI) studies the collective behavior of decentralized, self-organized natural or artificial systems. *SI* models consist typically in a population of simple agents interacting locally each other and with their environment. The agents follow very simple rules and, although there is no centralized control structure dictating how individual agents should behave, local interactions between such agents, often affected by a certain degree of randomness, lead to a complex intelligent emergent global behavior, with effects that would not have been expected by each individual.

Particle Swarm Optimization (PSO) is a population-based stochastic optimization algorithm, introduced in 1995 by Kennedy & Eberhart [5], which searches for an optimal solution in the computable search space [4]. This technique results in a metaheuristic for solving non-linear optimization problems. Generally, such problems cannot be solved exactly by an explicit method because in practice the mathematical expression of the objective function, also called fitness function, $f:\Omega \rightarrow \Re$ is not available. Instead of computing the optimum position $x^* \in \Omega$, a sufficiently good not necessarily optimal point $\hat{x} \in \Omega$, called sub-optimal solution, is obtained by a metaheuristic in the given search space Ω. *PSO* can also be seen as an evolutionary technique which, in contrast to Genetic Algorithms (*GA*s) and traditional Evolutionary Strategies (*ES*s) that use the competitive characteristics of biological survival, exploits cooperative and social aspects. Starting from a widely diffused population (swarm), individual components (particles) tend to move through the search space, eventually clustering in regions where minima are identified. Briefly, *PSO* simulates natural movement evolution for searching a solution with higher quality.

Computationally, a swarm consists of N artificial particles. The i^{th} particle $\mathbf{x}_i, i = 1,\ldots,N$, moves on the basis of a velocity vector $\mathbf{v}_i$, which is a function of the best position $\mathbf{p}_i$ found by the particle (i.e., local best solution) and of the global best position $\mathbf{g}$ found so far among all particles (i.e., global best solution). $\mathbf{x}_i$, $\mathbf{v}_i$, $\mathbf{p}_i$ and $\mathbf{g}$ are n-dimensional vectors, according to the space dimension. At iteration t, the position of the i^{th} particle is updated as follows:

$$\begin{cases} \mathbf{v}_i(t) = \underbrace{w(t)\mathbf{v}_i(t-1)}_{\text{inertial component}} + \underbrace{c_{\text{cog}} r_{1_{i,t}} \left(\mathbf{p}_i(t-1) - \mathbf{x}_i(t-1)\right)}_{\text{cognitive component}} + \underbrace{c_{\text{soc}} r_{2_{i,t}} \left(\mathbf{g}(t-1) - \mathbf{x}_i(t-1)\right)}_{\text{social component}} \\ \mathbf{x}_i(t) = \mathbf{x}_i(t-1) + \mathbf{v}_i(t) \end{cases}, \quad (3)$$

where $w(t)$ is the inertia weight, c_{cog} and c_{soc} are respectively the cognitive and the social acceleration constants; $r_{1_{i,t}}$ and $r_{2_{i,t}}$ are two uniformly distributed random numbers in the interval $[0,1]$. These parameters are set empirically, so representing the heuristic knowledge associated to the specific problem. Moreover, to keep $\mathbf{x}_i$ values within reasonable bounds, velocities are clamped into a symmetric range defined by a preset maximum velocity $\mathbf{v}_{\max}$: $\mathbf{v}_i \in [-\mathbf{v}_{\max}, \mathbf{v}_{\max}]$.

The update rule in (3) combines three different trends of movement:

- the inertia movement $w(t)\mathbf{v}_i(t-1)$, where $w(t)$ is the inertia weight and controls the influence of the move direction on the future motion;
- the cognitive movement $c_{\text{cog}} r_{1_{i,t}} \left(\mathbf{p}_i(t-1) - \mathbf{x}_i(t-1)\right)$, where $c_{\text{cog}} \in [0,2]$ is a constant that controls the particle cognitive behavior with probability $r_{1_{i,t}} \in [0,1]$, which is a scalar drawn at random for the i^{th} particle at each iteration;
- the social movement $c_{\text{soc}} r_{2_{i,t}} \left(\mathbf{g}(t-1) - \mathbf{x}_i(t-1)\right)$, where $c_{\text{soc}} \in [0,2]$ is a constant that controls the particle social skill with probability $r_{2_{i,t}} \in [0,1]$, which is a scalar drawn at random for the i^{th} particle at each iteration.

Summarizing, the particle is able to memorize its own best position $\mathbf{p}_i$ from the past, thus creating a kind of "nostalgia" to return there. When the fitness function $f(\cdot)$ is to be maximized, if $f(\mathbf{x}_i(t)) > \mathbf{p}_i(t-1)$, then $\mathbf{p}_i(t) = \mathbf{x}_i(t)$, otherwise the previous individual best position $\mathbf{p}_i(t-1)$ is kept. On the other hand, the particle $\mathbf{x}_i$ has also a social behavior, because it follows the swarm in its global best position $\mathbf{g}(t) = \arg\max_{\forall \mathbf{p}_i(t)} \{f(\mathbf{p}_i(t))\}$.

Similarly to all other metaheuristics, *PSO* is highly dependent on the parameter settings: the number of particles N; the inertia weight $w(t)$; the acceleration constants c_{cog} and c_{soc}; the maximum number of iterations $T_{\max}$. Moreover, the initial distribution of the population on the search space must be assigned. A suitable value for the inertia weight w usually provides balance between global and local exploration abilities, resulting consequently in a reduction of the number of iterations required to find the optimal solution. However, experimental results indicated that it is better to initially set w to a large value, in order to promote global exploration of the search space, and gradually decrease it to get more refined solutions [12]. Accordingly, a variable inertia weight $w(t)$ is usually defined as a monotonically decreasing function of the iteration t, such as in [11].

In addition to the basic *PSO* algorithm, several modifications are possible in order to enhance the achieved results:

- the best position in a neighborhood of each particle $\mathbf{x}_i$ could be considered, named $\mathbf{p}'_i$, instead of the global best position $\mathbf{g}$ [13]. Therefore, $\mathbf{p}'_i$ has to be substituted for $\mathbf{g}$ in the updating rules (3);
- evolution strategies can also be integrated, giving rise to a *hybrid PSO*. *GA* operators, such as mutation and crossover, can be used to preserve exploration capability in the various iterations, especially in the later stage of the evolution process [14]. Such a case could occur even at the early stage for a particle that is very close to the global best position $\mathbf{g}$, and the velocity will tend to zero. To avoid premature convergence and stagnation, after the particle positions updating, pairs of particles are selected for crossover with probability p_c, which is a random number generated uniformly in the interval $[0,1]$. For each pair, two child particles are generated by a crossover rule and replace their parents, maintaining the population size N constant [11]. The authors of [15] proposed the following crossover rule for parents $\mathbf{x}_i$ and $\mathbf{x}_j$, with $i \neq j$:

$$\begin{cases} \mathbf{x}'_i = p_c \mathbf{x}_i + (1-p_c)\mathbf{x}_j \\ \mathbf{x}'_j = p_c \mathbf{x}_j + (1-p_c)\mathbf{x}_i \end{cases}. \qquad (4)$$

  The velocities $\mathbf{v}_i$ and $\mathbf{v}_j$ are also updated from the velocities of the parents $\mathbf{v}'_i = \mathbf{v}_i V$, $\mathbf{v}'_j = \mathbf{v}_j V$, where: $V = (\mathbf{v}_i + \mathbf{v}_j) / \|\mathbf{v}_i + \mathbf{v}_j\|$.
- grouping the particles into subpopulations is a further alternative. Any clustering method can be used to perform this subdivision. Another random number p_{sp_c} is specified to represent the probability of intra-population crossover. Crossover among different subpopulations occurs with probability $1 - p_{sp_c}$;
- a constriction coefficient χ was also introduced to control the movement of $\mathbf{x}_i$, by balancing both convergence and explosive particle movements [16]:

$$\begin{cases} \mathbf{v}_i(t) = \chi[w(t)\mathbf{v}_i(t-1) + c_{\text{cog}} r_{1_{i,t}} (\mathbf{p}_i(t-1) - \mathbf{x}_i(t-1)) \\ \qquad + c_{\text{soc}} r_{2_{i,t}} (\mathbf{g}(t-1) - \mathbf{x}_i(t-1))] \\ \chi = \dfrac{2\kappa}{\left|2 - \varphi - \sqrt{\varphi^2 - 4\varphi}\right|}, \quad \varphi = c_{\text{cog}} + c_{\text{soc}}, \ \varphi > 4, \ \kappa \in [0,1] \end{cases}. \qquad (5)$$

III. Multimodal Biomedical Image Registration Approaches Based on PSO

In this section, multimodal medical image registration approaches that use *PSO* as searching strategy are described and critically reviewed. First, the introduction of an initial orientation term in the *PSO* formulation is explained. Then, the different *PSO* modifications are described.

A. Introduction of an Initial Position in the Standard PSO Formulation

In a large amount of the optimization techniques, such as *PSO*, standard test functions are employed for benchmark testing and continuous optimization algorithms assessment. In these cases, the initial set of parameters has little importance. However, in many practical applications, there is usually at least some knowledge of the characteristics of $\mathbf{x}^*$ for which $f(\mathbf{x}^*)$ is the global optimum [11]. This situation is certainly true in biomedical image registration, since the users of clinical imaging systems are generally skilled physicians. These clinicians can supply a trustworthy indication of the correct orientation, by choosing an accurate initial transformation. Although co-registration is required because of both medical image complexity and human subjectivity or error, registration algorithms can definitely benefit from an accurate initial guess.

This may also occur with *PSO*, as $\mathbf{v}_{\max}$ and constriction coefficient χ only prevent particle straying from the region of feasible solutions. However, if the particles $\mathbf{x}_i$ were arranged according the user's initial orientation, while swarming, they may have a higher probability of discovering a region that contains $\mathbf{x}^*$. Briefly, in addition to the swarming effect around the current global best $\mathbf{g}$ and each particle recollection of its personal best $\mathbf{p}_i$, the initial orientation $\mathbf{x}_{\text{init}}$ can be also introduced into the velocity $\mathbf{v}_i$ of each particle [11]. The formulation in (3) is modified to (6):

$$\begin{cases} \mathbf{v}_i(t) = w(t)\mathbf{v}_i(t-1) + c_{\text{cog}} r_{1_{i,t}} (\mathbf{p}_i(t-1) - \mathbf{x}_i(t-1)) \\ \qquad + c_{\text{soc}} r_{2_{i,t}} (\mathbf{g}(t-1) - \mathbf{x}_i(t-1)) + c_{\text{ret}} r_{3_{i,t}} (\mathbf{x}_{\text{init}} - \mathbf{x}_i(t-1)). \\ \mathbf{x}_i(t) = \mathbf{x}_i(t-1) + \mathbf{v}_i(t) \end{cases} \qquad (6)$$

where c_{ret} is the acceleration constant for returning to the initial orientation and $r_{3_{i,t}}$ is a uniformly distributed random number in $[0,1]$. Eq. (5) is also revised accordingly.

Stochastic and evolutionary global optimization techniques, including *PSO*, can generally discover the promising region or the "basin of attraction" in the search landscape. However, they typically exhibit slow convergence to $\mathbf{x}^*$, even though the complexity of similarity metric computation needs fast convergence. For these reasons, a local method is applied to the best point in the promising region found by the *PSO* [11]. *Powell's direction set algorithm* is very appropriate for this purpose, because it does not require derivative computation [10].

B. Versions of Biomedical Image Registration Approaches using PSO

Several literature works have addressed the issues related to biomedical image registration using *PSO*. For simplicity and compactness, the pseudo-code of the biomedical image registration process based on the standard *PSO* technique, using a rigid-body model, is reported in Algorithm I box. In addition to the "traditional" plain *PSO*, other versions, including initial orientation knowledge and/or *ESs*, have been proposed in the literature. These more advanced registration approaches aim to balance between exploration and exploitation, avoiding premature convergence.

In [11], three main variants of biomedical image registration based on *PSO* are described and compared: *(i) Hybrid PSO with crossover operators* for positions and velocities updating [15]. However, for normal velocity updates, (5) is exploited. Convergence criteria are $T_{\text{NoImprove}} = 20$ iterations in which there is no improvement in $f(\mathbf{g})$, or reaching the maximum number of iterations $T_{\max}$. After the *PSO* convergence, Powell's local optimization method is applied to the best point in the swarm; *(ii) Hybrid PSO with crossover and subpopulations*, analogous to the previous one except that five subpopulations were initially determined with the K-Means clustering algorithm. Additionally, after convergence, Powell's method is applied to the best points in each subpopulation, resulting in the final registration transformation; *(iii) PSO with constriction coefficient and relaxed convergence criteria* is the most "controlled" of the three techniques. A "loose" local optimization with Powell's method is applied to $\mathbf{x}_{\text{init}}$, resulting in $\mathbf{x}'_{\text{init}}$ around which particles are generated. *PSO* with constriction factor χ is applied, the velocities are updated according to (6) combined with (5) and convergence criteria are more relaxed. If in some iteration $f(\mathbf{x}_i) < f(\mathbf{g})$, then $\mathbf{g}$ is set to $\mathbf{x}_i$, but if $\|\mathbf{x}_i - \mathbf{g}\| < \varepsilon$ the iteration is still considered to be a non-improving iteration. Convergence is faster, as the iteration counter is not reset to zero for improving points very close to $\mathbf{g}$. Powell's local optimization is applied to $\mathbf{g}$ after the convergence (a function value change less than 0.005).

Although the constriction coefficient prevents the particles from straying out of the space of feasible solutions, the particles have a greater probability of being drawn out of local optima by the additional term.

ALGORITHM I. PSEUDO-CODE OF THE BIOMEDICAL IMAGE REGISTRATION PROCEDURE USING PLAIN PSO. RIGID-BODY TRANSFORMATIONS AND MUTUAL INFORMATION (MI) SIMILARITY METRIC WERE EMPLOYED.

Input: Source (floating) image: A
Reference (fixed) image: B
Output: Estimation of the best transformation:
$$\hat{\mathbf{T}} = \arg\max_{\mathbf{T}\in\Omega} \{ I(\mathbf{T}(A), B) \}$$
Image A aligned with the image B: $\hat{\mathbf{T}}(A)$
Parameters: Parameter vector to be estimated:
$$\mathbf{x} = (t_x, t_y, t_z, \alpha, \beta, \gamma)$$
Inertia weight: w
Acceleration constants: $c_{\text{cog}}, c_{\text{soc}}$
Total number of particles: N
Min improvement in *MI* between two consecutive iterations: ε
Max number of iterations: $T_{\max}$

/* Initialization of the population */
for each particle $i \in \{1,2,\ldots,N\}$ **do**
  Set particle position $\mathbf{x}_i(0)$ at random;
  Set particle velocity $\mathbf{v}_i(0)$ at random;
  $\mathbf{p}_i(0) \leftarrow \mathbf{x}_i(0)$;
end for
$\mathbf{g}(0) \leftarrow \arg\max_{\forall \mathbf{p}_i(0)} \{ f(\mathbf{p}_i(0)) \}$;
/ Iterate until the convergence condition is achieved */*
while($f(\mathbf{g}(t-1)) - f(\mathbf{g}(t-2)) \geq \varepsilon$ **and** $t \leq T_{\max}$) **do**
  for each particle $i \in \{1,2,\ldots,N\}$ **do**
    / Velocity and position updating */*
    $\mathbf{v}_i(t) \leftarrow w\mathbf{v}_i(t-1) + c_{\text{cog}} r_{1_{i,t}} (\mathbf{p}_i(t-1) - \mathbf{x}_i(t-1)) + c_{\text{soc}} r_{2_{i,t}} (\mathbf{g}(t-1) - \mathbf{x}_i(t-1))$;
    $\mathbf{x}_i(t) \leftarrow \mathbf{x}_i(t-1) + \mathbf{v}_i(t)$;
    / Particle movement and fitness evaluation */*
    if $f(\mathbf{x}_i(t)) > \mathbf{p}_i(t-1)$ **then**
    / Better solution according to MI maximization */*
    / Update the current particle best solution */*
      $\mathbf{p}_i(t) \leftarrow \mathbf{x}_i(t)$;
    else
      / Keep the previous particle best solution */*
      $\mathbf{p}_i(t) \leftarrow \mathbf{p}_i(t-1)$;
    end if
  end for
  / Global best position updating */*
  $\mathbf{g}(t) \leftarrow \arg\max_{\forall \mathbf{p}_i(t)} \{ f(\mathbf{p}_i(t)) \}$;
  / Iteration counter increment */*
  $t \leftarrow t+1$;
end while

The authors of [11] stated that the modifications were designed *ad hoc* for image registration and this term improved registration accuracy. In other applications, however, there may be no prior knowledge of the location of the global optimum. In these cases, the last version may prevent particles from moving towards the global optimum, and (3) should be used for velocity update. If a feasible region, wherein the correct transformation likely lies, cannot be identified, then the other *PSO* hybridizations (i.e., the use of crossover and subpopulations) are recommended.

Some knowledge of the correct orientation can greatly improve the search. Both the initial orientation term and the constriction coefficient prevent the search from straying too far from the global optimum. Hybridization with *ES* operators appears to improve accuracy by diversifying particle locations. As shown in the last version, convergence criteria during the global search can be relaxed, as local optimization can find the global optimum if a particle is sufficiently close to it.

The authors of [17] investigated four different plain *PSO* versions for the registration of the images, without integrating other optimization approaches: *(i) Standard PSO* corresponds to the standard *PSO* introduced in 2007 by Bratton & Kennedy [18]; *(ii) Standard PSO with variable inertia weight* represents a modification of the earlier described standard *PSO* based on [11], where the inertia weight $w(t)$ monotonically decreases during the iterations; *(iii) Standard PSO with initial orientation, relaxed convergence criteria and constriction coefficient* is another alteration presented by Wachowiak *et al.* [11]. This version includes the initial orientation of the volumes to one another, according to (6) and (5); *(iv) PSO with constriction coefficient, relaxed convergence criteria and variable influence of the initial orientation* is a modification of the previous version. Since the involvement of the initial orientation can prevent the convergence of the swarm, the influence of the component $\mathbf{x}_{\text{init}}$ in (6) should decrease in each iteration:

$$\begin{cases} c_{\text{soc}}(t) = c_{\text{soc}}(t-1) - \Delta\varphi \\ c_{\text{ret}}(t) = c_{\text{ret}}(t-1) + \Delta\varphi \\ \varphi = c_{\text{cog}} + c_{\text{soc}} + c_{\text{ret}} \\ \Delta\varphi = \dfrac{c_{\text{ret}\min} - c_{\text{ret}\max}}{T_{\max}} \xrightarrow{c_{\text{ret}\min}=0} \Delta\varphi = \dfrac{-c_{\text{ret}\max}}{T_{\max}} \end{cases} . \tag{7}$$

Chen et *al.* [19][20] investigated an extension of the *PSO* to a *Hybrid Particle Swarm Optimizer (HPSO)*, by integrating two methods from the *GA*s into the standard *PSO*. The authors argued that classical *PSO* is convenient for 2D-2D registration, but is less efficient for 3D-3D alignment. They solved this problem by using a hybrid algorithm. The chosen optimization metric is again *MI*.

An alternative non-linear 2D-2D affine registration technique for MR and CT modality images of human brain sections was presented in [21], using a correlation function as objective function. Both *GA* and *PSO* schemes were considered in a multiresolution domain (using Haar wavelet transform) to decrease the sensitivity of the registration procedure to local maxima and achieve an idea of the initial orientation of the images to be registered. A comparative study analyzed the results.

IV. Experimental Findings

An accurate and fair comparison among the different literature approaches is not so straightforward because different medical datasets were used in experimental trials, due to the unavailability of public medical benchmarks for intensity-based image registration. In addition, all the approaches used a small number of images for 2D or 3D registration tests, making the experimental findings much less significant.

As first experimental evidence, in Das & Bhattacharya [21], *PSO* approach resulted more accurate and efficient for biomedical image registration than *GA* and other evolutionary techniques, considering the correlation value. As a matter of fact, *PSO* in its basic form is best suited for continuous variables, allowing to evaluate more precisely the objective function, while *GA*s work better in discrete search spaces. Consequently, *PSO* outperforms *GA*s in image registration application. Moreover, the considerable adaptability due to stochastic exploration and exploitation of the swarm strengthens *PSO* over other robust optimization techniques. Good convergence result has been obtained with a population size of $N = 20$ particles using both optimization techniques.

In Wachowiak *et al.* [11], experiments consisted in registering single 2D slice biomedical images to 3D volumes. This 2D-to-3D medical image registration can be useful for real-time monitoring, when an intra-treatment slice has to be aligned with a pre-treatment 3D dataset. Unfortunately, only three clinical instances, including also synthesized MRI and ultrasound images, were considered: three 3D volumes, and four 2D images to be registered with each volume. In these experimental trials, a population size of $N = 35$ particles was used. It was shown that incorporating the initial position into the velocity update equation increased registration accuracy significantly. Moreover, hybrid *PSO-ES* and *PSO* incorporating the constriction coefficient produced the highest percentage of correct registrations among all the tested *PSO* techniques. In comparisons, the *PSO* methods were noticeably more accurate than the other *ES* techniques.

The authors of [17] developed plain *PSO* in four different modifications for the registration of the images, without the influence of another optimization method. The prior presented test results showed that the classical *PSO* versions reach their limits for the given optimization problem. On the other hand, the two *PSO* versions with influence of the initial orientation reported much better results.

In the experiments performed in [19][20], standard *PSO* and hybrid *PSO* were compared against conventional gradient descent method as well as a *GA*. The optimization methods were used for rigid registration of 3D image data. *HPSO* achieved the best results among the approaches for both rigid and non-rigid registrations. *PSO* outperformed the gradient descent procedure and the *GA*. However, exact quantities and parameters used during the trials are not reported.

Opposing findings and opinions have been found in the literature, especially in [19][20] and [17]. Chen *et al.* claimed in their articles [19][20] that plain *PSO* is just convenient for 2D-2D registration, while for higher dimensions a hybrid method should be used. The results obtained in [17] contradicted the ones in [19], because it was shown that the alignment of 3D data was possible using the plain *PSO* without combining other optimization methods. Regarding performance speed-up, both plain *PSO* and hybrid *PSO* with *ES*s are inherently parallel, and the computation times can be greatly improved by using either distributed or shared memory architectures. Finally, both accuracy and efficiency of the *PSO* methods could be further improved by additional modifications, such as more sophisticated swarm initialization strategies [22].

V. DISCUSSION AND CONCLUSIONS

In this paper a critical review of the literature works concerning biomedical image registration approaches using *Particle Swarm Optimization* was presented.

Swarm Intelligence techniques have been shown to be very efficient and powerful in a wide variety of computer science areas. Depending on the problem nature, continuous or discrete search spaces can be properly defined. Accordingly, the different *SI* approaches, such as *PSO*, may provide more efficient solution encoding either in continuous or discrete optimization problems. However, although each optimization technique was first designed for a particular purpose, the majority of evolutionary algorithms were adapted from continuous to discrete search space, and vice versa. The *Bat Algorithm (BA)* [23] can be seen as a hybridization of *PSO* and a local search. *BA* achieves better results with respect to *PSO* when a large number of parameters must be estimated [24]. Elastic registration problem could be properly treated with *BA* because of the thousands of parameters to be optimized. However, no literature work has addressed yet this challenging issue using *SI* techniques.

In conclusion, although more accurate comparisons must be made with other global and local optimization paradigms, *Particle Swarm Optimization* achieves encouraging results in biomedical image registration. This approach deserves certainly further study and represents a promising open research issue for multimodal medical image registration.

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