Identifying Metastasis in Bone Scans with Stochastic Diffusion Search

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***Abstract*—This paper introduces the use of a swarm intelligence algorithm – Stochastic Diffusion Search – as a tool to identify metastasis in bone scans. This algorithm is adapted for this particular purpose and its performance is investigated by running the algorithm's agents on sample bone scans whose status have been determined by the experts. A statistical analysis is also presented, highlighting the behaviour of the algorithm when presented with different samples.**

I. Introduction

Computer aided diagnosis (CAD) is an emerging field in medicine. This technique can help the radiologist to examine the image in greater depth and has the potential to help doctors from different medical disciplines to interpret medical imaging with greater confidence. Furthermore CAD is a promising learning tool for both medical students and junior doctors to develop basic diagnostic skills. This paper presents a new CAD approach in which a swarm intelligence algorithm – Stochastic Diffusion Search (SDS)[1] – is tested to detect areas of high technetium-99m–labeled diphosphonates on bone scans.

Communication – social interaction or information exchange – observed in social insects is important in all swarm intelligence algorithms, including Stochastic Diffusion Search (SDS)[1], which mimics the recruitment behaviour of one species of ants – *Leptothorax acervorum*. Although as stated in [2], in real social interactions, not just the syntactical information is exchanged between the individuals but also semantic rules and beliefs about how to process this information, in swarm intelligence algorithms only the syntactical exchange of information is considered.

There are different forms of recruitment in social insects: it may take the form of local or global, one-to-one or one-to-many, and stochastic or deterministic mode. The nature of information exchange also varies in different environments and with different types of social insects. Sometimes, the information exchange is more complex where, for example, it might carry data about the direction, suitability of the target and the distance; sometimes the information sharing is simply a stimulation forcing a certain triggered action. What all these recruitment and information exchange strategies have in common is distributing useful information in their community.

This paper starts by describing the standard Stochastic Diffusion Search, followed by an introduction to bone scintigraphy, explaining metastatic disease and a brief explanation on how to detect metastasis in bone scans. Afterwards, the swarm intelligence algorithm is adapted for the purpose of this research, the results is reported and a statistical analysis is presented demonstrating the performance of the approach.

It is vital to note that the presented approach is not attempting to replace the experts' eyes of radiologists, but rather to aid them in the diagnosis process. The software has been used as an educational tool on several occasions to teach medical students and junior doctors.

II. Stochastic Diffusion Search

This section introduces Stochastic Diffusion Search (SDS) [1] – a swarm intelligence algorithm – whose performance is based on simple interaction of agents.

The SDS algorithm commences a search or optimisation by initialising its population and then iterating through two phases (see Algorithm 1)

Algorithm 1 SDS Algorithm

```
01: Initialising agents()
02: While (stopping condition is not met)
03:    Testing hypotheses()
04:       Determining agents' activities (active/inactive)
05:    Diffusing hypotheses()
06:       Exchanging of information
07: End While
```

In the test phase, SDS checks whether the agent hypothesis is successful or not by performing a hypothesis evaluation which returns a boolean value. Later in the iteration, contingent on the precise recruitment strategy employed (in the diffusion phase), successful hypotheses diffuse across the population and in this way information on potentially good solutions spreads throughout the entire population of agents. In other words, each agent recruits another agent for interaction and potential communication of hypothesis. This algorithm has been used alongside other swarm intelligence algorithms in several fields (e.g. [3], [4], [5], [6]).

A. Standard SDS and Passive Recruitment

In standard SDS (which is used in this paper), *passive recruitment mode* is employed. In this mode, if the agent is

inactive, a second agent is randomly selected for diffusion; if the second agent is active, its hypothesis is communicated (*diffused*) to the inactive one. Otherwise there is no flow of information between agents; instead a completely new hypothesis is generated for the first inactive agent at random (see Algorithm 2). Therefore, recruitment is not the responsibility of the active agents. In this work, activity of each agent is determined when its fitness is compared against a random agent (which is different from the selecting one); if the selecting agent has a better fitness (smaller value in minimisation problems) than the randomly selected agent, it will be flagged as active, otherwise inactive. Higher rate of inactivity boosts exploration, whereas a lower rate biases the performance towards exploitation.

Algorithm 2 Passive Recruitment Mode

```
01: For ag = 1 to No_of_agents
02:    If ( !ag.activity() )
03:       r_ag = pick a random agent()
04:       If ( r_ag.activity() )
05:          ag.setHypothesis( r_ag.getHypothesis() )
06:       Else
07:          ag.setHypothesis( randomHypothesis() )
08:       End If/Else
09:    End If
10: End For
```

III. Bone Scintigraphy

Bone scan or Bone scintigraphy is one of the most frequently performed of all radionuclide procedures. Radionuclide bone imaging is quick, relatively inexpensive, widely available, and exquisitely sensitive and is invaluable in the diagnostic evaluation of numerous pathologic conditions. Although protocols vary among institutions, imaging is typically performed 26 hours after intravenous administration of technetium-99m–labeled diphosphonates. The delay between injection and imaging allows clearance of the radiotracer from the soft tissues, resulting in a higher target-to-background ratio and improved visualization of bone. The degree of radiotracer uptake depends primarily on two factors: blood flow and, perhaps more importantly, the rate of new bone formation [7].

A. Normal Scintigraphic Findings

There is symmetric distribution of activity throughout the skeletal system in healthy adults. Urinary bladder activity, faint renal activity, and minimal soft-tissue activity are also normally present (see Fig. 1 Top-left).

The accumulation of radiotracer in bone generally decreases with age. However, there are sites of persistently increased symmetric uptake, such as the acromial and coracoid processes of the scapulae, the medial ends of the clavicles, the junction of the body and manubrium of the sternum (angle of Louis), and the sacral alae. Increased radiotracer accumulation in the jaw may be due to dental disease or to malocclusion of dentures.

Symmetric areas of increased calvarial activity occurs in hyperostosis frontalis. In the neck, activity in calcified thyroid cartilage and in the apophyseal joints of the cervical vertebrae in patients with asymptomatic degenerative changes can also be seen.

B. Metastatic Disease

Metastasis is the process by which the cancer spread from the original site at which it started as a primary tumour to other tissues in the body i.e. Prostate cancer metastasizing to the bone tissue.

Many if not most bone scans are performed in patients with a diagnosis of cancer, especially carcinoma of the breast, prostate gland, and lung. Radionuclide bone imaging plays an imporant part in tumor staging and management. This imaging technique is extremely sensitive for detecting skeletal abnormalities, and numerous studies have confirmed that it is considerably more sensitive than conventional radiography for this purpose [8]. About 75% of patients with malignancy and pain have abnormal bone scintigraphic findings. The usual pattern consists of increased radiotracer deposition in areas of new bone tissue formation in response to the damaging effect of cancer on the bone [8], [9]. The presence of multiple, randomly distributed areas of increased uptake of varying size, shape, and intensity are highly suggestive of bone metastases (see Fig. 1 Top-middle). Although multiple foci of increased activity may be encountered in other pathologic conditions, it is often possible to distinguish metastatic disease from other entities by analyzing the pattern of distribution of the abnormalities. Traumatic injury, in contrast to metastatic disease, generally manifests as discrete focal abnormalities of similar intensity. In older patients, osteoarthritis and degenerative changes may manifest as areas of intense activity on radionuclide bone images. These changes can be distinguished from metastatic disease by virtue of their characteristic location (e.g. knees, hands and wrists). Involvement of both sides of the joint is common in arthritis but unusual in malignant conditions [10].

When the metastatic process is diffuse, virtually all of the radiotracer is concentrated in the skeleton, with little or no activity in the soft tissues or urinary tract. The resulting pattern, which is characterized by excellent bone detail, is frequently referred to as a superscan (see Fig. 1 Top-right) [9], [10], [11].

Bone scintigraphy is a popular and important imaging modality and will likely remain so for the foreseeable future. Although bone scintigraphy is not specific, its exquisite sensitivity makes it a useful screening procedure for many pathologic conditions, especially for the detection of prostate, breast and lung cancer metastasis.

C. Swarm Intelligence and Bone Scans

In the current paper we are presenting unique approach by deploying SDS to detect the bone metastasis. This approach demonstrates a promising ability to undertake this task with similar level of sensitivity. Each scan in Fig. 1 (Top) are processed by the SDS agents which are responsible for locating the affected area(s). According to the description given in the

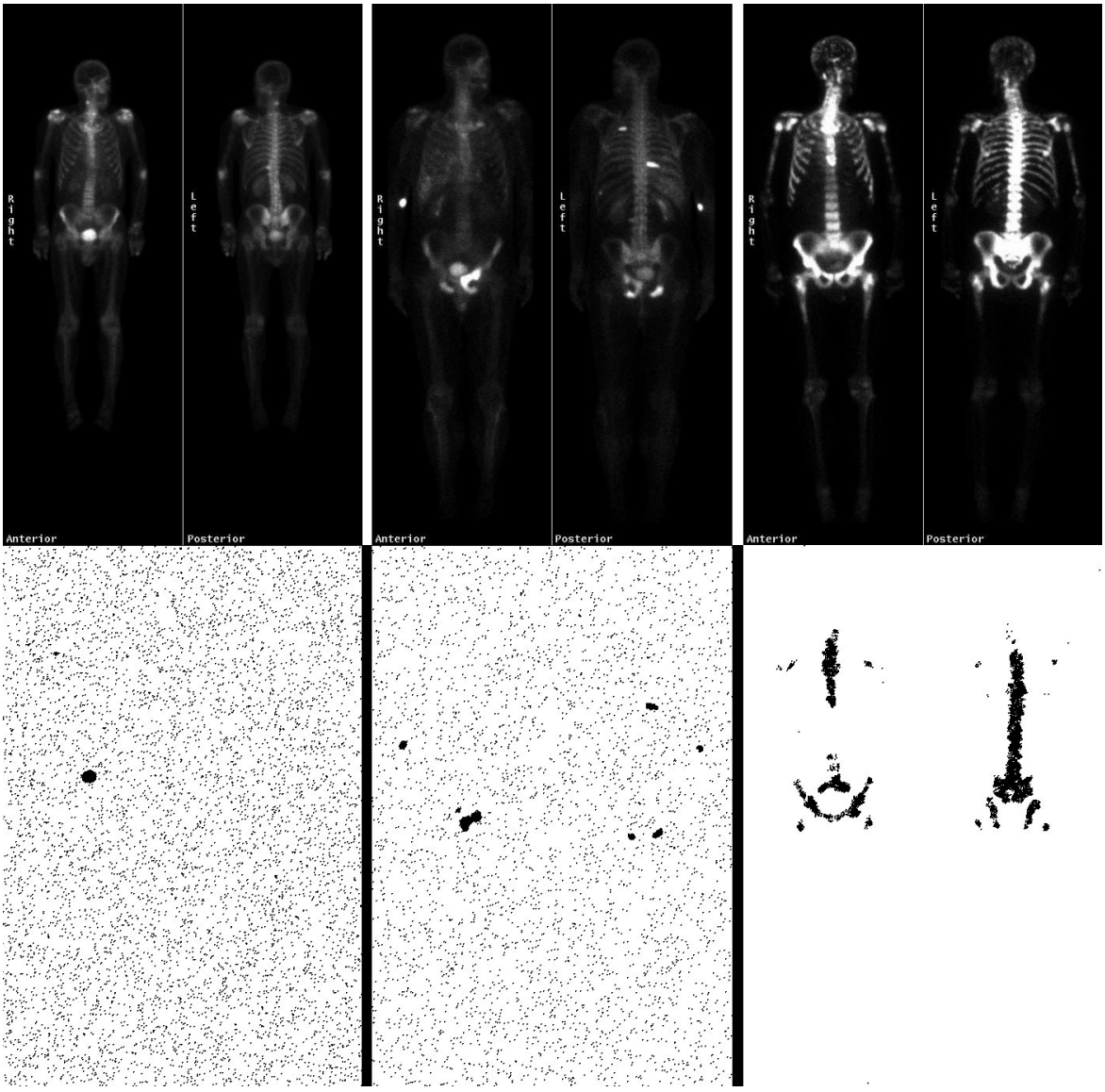

Fig. 1. Bone Scans
Top: Typically 2–6 hours after intravenous administration of technetium-99m–labeled diphosphonates. Brigher areas indicate a higher radiotracer uptake.
Bottom: The scans are processed using Stochastic Diffusion Search algorithm.
Left: Healthy; middle: partially affected; right: metastatic disease spread.

previous section, Fig. 1 (Top-middle and right) are the areas of metastasis.

The reproducibility and the accuracy of the SDS algorithm can be utilised in developing a standardised system to interpret the bone scans preventing operator errors and discrepancies. This technology can be employed as an adjunct by radiologists to assess the various parts of the bone scan making the diagnosis of the lesions more thorough and less time consuming. Additionally this technique can be effectively used to develop programs for teaching and training medical students and junior doctors.

IV. Experiments

This section presents the technical details and the experiment setup, followed by the results and a statistical analysis of the performance of the algorithm.

The number of agents used in this experiment is 10,000 and the algorithm is run for 10 iterations (i.e. 10 cycles of test and diffusion phases).

As stated earlier in Section II, in the beginning of the process, all the agents are initialised randomly throughout the search space. In other words, each agent randomly picks a pixel from the image of the bone scan (i.e. one pixel from 460×690). During the test phase of SDS algorithm, each

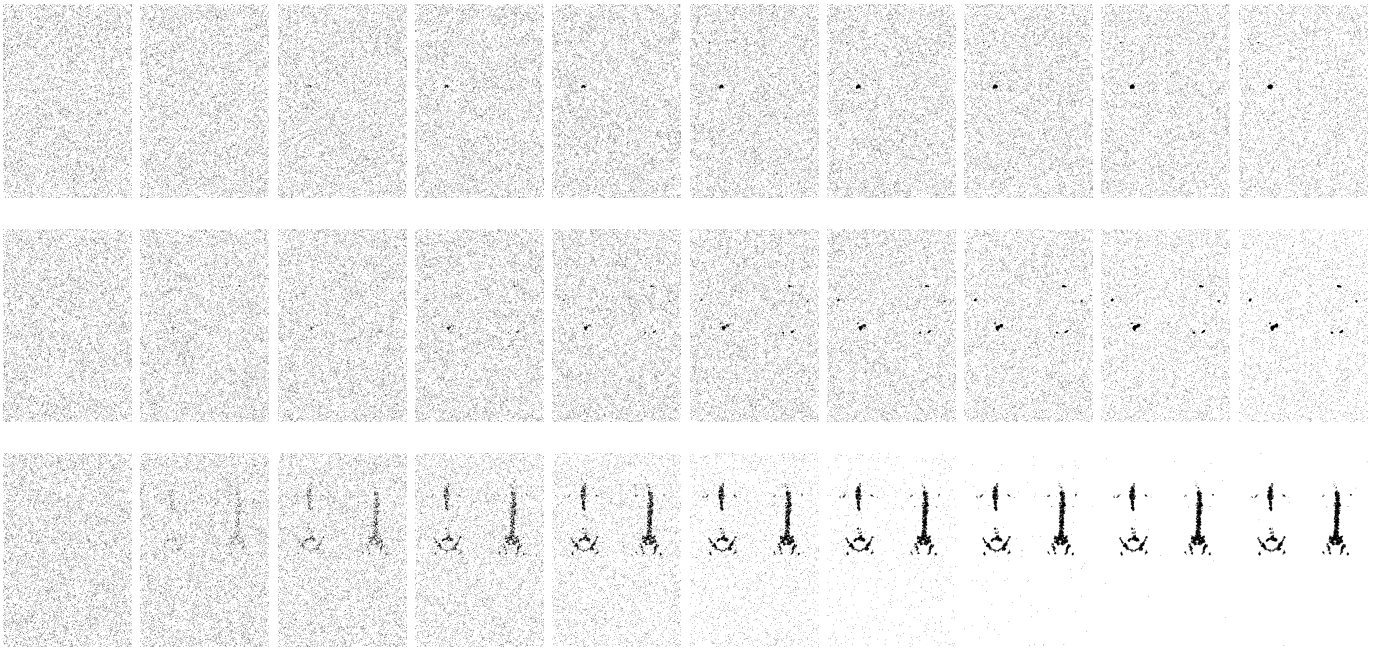

Fig. 2. SDS Algorithm Processing Bone Scans in 10 Iterations

Each row shows the behaviour of the agents when presented with one bone scan. Each bone scan is processed by 10,000 agents (illustrated as black dots) and through communication, agents explore different areas of the bone scan to identify potential areas of metastasis. The leftmost figures in each row show the location of the agents on the first iteration, and the rightmost ones represent the last iteration.

Top: Healthy; middle: partially affected; bottom: metastatic disease spread.

o	o	o
o	x	o
o	o	o

Fig. 3. Agent's Neighbours in Test Phase

The symbol x represents the position of the agent and the o's represent the neighbours used during the test phase.

agent's status should be determine. The method used here to set the activity of the agents is to find the average of the colour intesity[1] ($avgIn$) of each agent and its neighbours (see Fig. 3). If $avgIn > 180$[2] the agent is flagged active, otherwise inactive.

During the diffusion phase, each inactive agent randomly selects another agent from the population; if the selected agent is active, the selecting agent adopts the hypothesis (i.e. location) of the active agent and the information sharing takes place. The strategy used for information sharing is to randomly pick an area surrounding the active agent (see Fig. 4). Active agents also check their position by continously picking a random pixel in the neighbourhood; this way, an area which does not have a good potential is discarded from one iteration to the next.

[1]By colour intensity, we mean the brightness of each pixel, which is a spectrum from 0 to 255.

[2]This value is problem-dependent and could be adjusted to increase or decrease the sensitivity of the system.

o	o	o	o	o
o	o	o	o	o
o	o	x	o	o
o	o	o	o	o
o	o	o	o	o

Fig. 4. Diffusion Area

The symbol x represents the position of the active agent and the o's represent the accessible places during the diffusion phase.

A. Results

As shown in Fig. 1 (Bottom), areas which higher potential of metastasis are identified. Other than urinary bladder activity, faint renal activity, and minimal soft-tissue activity which are normally present in the scan (Fig. 1 Bottom-left), the existence of multiple, randomly distributed areas of increased uptake of varying size, shape, and intensity are highly suggestive of bone metastases (Fig. 1 Bottom-middle). Additionally as stated before, when the metastatic process is distributed, almost all of the radiotracer congregates in the skeleton, with little or no activity in the soft tissues or urinary tract (Fig. 1 Bottom-right).

In order to show the behaviour of the algorithm in each iteration, the position of each one of the agents over the process of metastasis identification is illustrated in Fig. 2. In this figure, the three original bone scans referred to earlier

are used as input to the system, and as the figure shows, successful agents diffuse their positions across the population and this way, information on potentially good solutions spreads throughout the entire population of agents. This process is caused through the recruitment strategy, where each agent recruits another agent for interaction and potential communication of the promising areas.

As a measure to decide whether the activity of the agents when presented with different types of bone scans (e.g. not affected, affected and highly affected), would be a distinctive indicator, a statisical analysis is run. TukeyHSD Test [12] is used to highlight whether there is a significant difference between the activity of the agents when processing the bone scans. Table I (a) shows the activity rate of the populations over each iteration. Three different samples are used for this analysis: Samples 1, 2 and 3, refer to the scans in Fig. 1 (left to right). Table I (b) shows that other than the first iteration where the agents are just initialised, different bone scans would result in significantly different activity rate in the agents. This could be used as an indicator that this method could help highlighting the difference between various scans and whether they are healthy, partially affected or the metastasis is spread.

V. Conclusion

The results of the novel application of Stochastic Diffusion Search to detect areas of metastasis in this experiment demonstrates that this approach can yield promising results. A statistical analysis further investigates the behaviour of the agents in the population and the outcome demonstrates that the algorithm exhibits a statistically significant difference when applied to bone scans for healthy, partially affected or heavily affected individuals. Finally the authors would like to emphasise that the presented technique could be effectively utilised as an adjunct to the experts' eyes of a specialist.

TABLE I
Activity Status of Agents

(a) Mean ±standard deviation of the number of active agents in each iteration is is shown (rounded to the nearest number).

Itr	Sample 1	Sample 2	Sample 3
0	0±0	0±0	0±0
1	5±2	17±4	277±16
2	15±4	47±9	763±37
3	33±8	100±18	1602±76
4	66±18	201±31	2991±137
5	129±33	379±51	4992±188
6	245±62	697±84	7260±198
7	461±110	1250±141	8947±123
8	852±201	2201±230	9583±51
9	1557±351	3650±330	9708±22

(b) Based on TukeyHSD Test, if the difference between each pair of samples is significant, the pairs are marked (o – X shows that the left sample has a significantly more active agents than the left one). This test uses 95% family-wise confidence level. The aim is to show that agents dealing with scans which have different levels of metastasis exhibit significantly different behaviour.

Itr	s1 – s2	s1 – s3	s2 – s3
1	–	–	–
2	o – X	o – X	o – X
3	o – X	o – X	o – X
4	o – X	o – X	o – X
5	o – X	o – X	o – X
6	o – X	o – X	o – X
7	o – X	o – X	o – X
8	o – X	o – X	o – X
9	o – X	o – X	o – X
10	o – X	o – X	o – X

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