A Distributed Artificial Immune Network for Optimizing Tracer Kinetic Models with MATLAB Distributed Computing Engine

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***Abstract*—artificial immune networks (AIN) as one of the new intelligent soft computing methods have been widely used in many application fields. The AIN shows good ability of global optimization, especially in parameter optimization of pharmacokinetic models. The AIN search global optimum based on the principles of clone selection and immune network. However, as one of the heuristic-based optimal algorithms, the evolution of memory cells in the AIN is time consuming compared with gradient-based optimal algorithms. In this paper, a distributed AIN with distributed clone selection evolutionary strategy is proposed to improve the efficiency of the AIN. Then a distributed artificial immune network is implemented with MATLAB Distributed Computing Engine. One of the advantages of MDCE is that it is easy to run optimal algorithms programmed in MATLAB platform. In the experiments, parameters of the [^{18}F] Fluoro-2-deoxy2D-glucose (FDG) tracer kinetic model are optimized with the distributed AIN. Experimental efficiency of the algorithm is discussed.**

Keywords-artificial immune network; tracer kinetic model; distributed computing; MDCE

I. INTRODUCTION

The artificial immune system [1] is a bio-inspired soft computing method. Artificial immune network (AIN) as a branch of artificial immune system -produces the interaction mechanism between network cells. The AIN algorithms have been successfully applied in multi-modal function optimization [2] and dynamic environment optimization [3]. In our previous work, a PKAIN algorithm has been proposed to optimize parameters of both linear and nonlinear pharmacokinetic compartmental models [14]. Compared with other artificial immune algorithms, the PKAIN is based on clonal selection evolution [1] and the simplex updates of the memory cells to implement optimization. However, the clonal selection evolution is one of the most time-consuming steps in each iterative updates of the PKAIN generations. In order to obtain global optimizations using the PKAIN algorithm, much more memory cells should be generated in the network. As a result, it costs much more time compared with those gradient-based optimal algorithms. In this paper, a distributed PKAIN using a distributed clonal selection evolutionary strategy is proposed to save working time for optimizing parameters of the compartment model function. The tracer kinetics model is to be done as an example of the distributed PKAIN to evaluate the efficiency of the distributed strategy analysis. The MATLAB Distributed Computing Engine (MDCE) is setting as an experimental platform. One of advantages of the MDCE is that it integrates both simple distributed function interfaces and the MATLAB programming functions. Experimental results show that the distributed PKAIN with MDCE can improve the efficiency of the artificial immune network. It keeps the accuracy and reduces time consuming when using for parameters optimization.

II. TRACER KINETIC MODELING

Tracer kinetic modeling with positron emission tomography (PET) requires measurements of the time activity curves in both plasma and tissue to estimate physiological parameters [4]. Dynamic PET images can be evaluated visually or quantified by tracer kinetic modeling, which uses a tracer plasma time-activity curve (PTAC) as an input function in order to characterize the target tissue time-activity curve (TTAC) for a predefined region of interest (ROI). This characterization is achieved using physiological parameters [5]. Compartmental model is the most commonly used model to describe the uptake and clearance of radioactive tracers in tissue [6]. In general, the body is considered to be a system, and the distribution kinetics of the tracer can be described as many compartments, which refer to organs or tissues where the rates of absorption and transportation are similar. So, an appropriate model to fit PTAC and TTAC

978-0-7695-4415-1/11 $26.00 © 2011 IEEE
DOI 10.1109/DCABES.2011.2

are most important. Firstly, a mathematical tracer kinetic model is selected based on the principle of pharmacokinetics. Then parameters of the model are optimized to fit the TTAC, PTAC curve. Currently fluorine generation of deoxidizing glucose (FDG) kinetic model [7] is relatively commonly used, as shown in Fig.1. The three compartments [15] four parameters model which is originally proposed by Sokoloff et al is used to describe metabolic process of FDG [4] . At first the FDG get into the tissue cells through the cell membrane, and then they are transformed into a FDG-6-P by sugar kinesis in cells, eventually captured by cells. Conversely, the reverse process is also feasible in the model. There are four parameters (called rate constants) $k_1 \sim k_4$ in the compartment model and they represent the tracer transport rate between compartments. The rate constant k_1 is measured in ml (g min)$^{-1}$, and k_2 , k_3 and k_4 are measured in min^{-1}. C_B , C_E and C_M represent FDG concentration in the plasma, FDG concentration in the tissue, and FDG-6-phosphate (FDG-6-P) concentration in the tissue, respectively. In addition, in tracer dynamics research this model has another parameter f , it represents the image in the PET that the influenced coefficients by the radioactivity in the plasma of the surrounding tissue imaging factor.

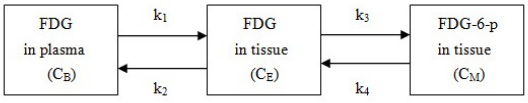

Figure 1. The FDG tracer kinetic model

The actual tissue activity measured by PET can be expressed as

$$C_T(t) = C_i(t) + f \cdot C_B(t) \quad (1)$$

Where $C_i(t) = C_E(t) + C_M(t)$, $C_T(t)$ is the function of tissue tracer time-activity curve (TTAC). Through calculate and optimize this model, we can get the following equation:

$$C_T(t) = k_1/(\alpha_2 - \alpha_1).[(k_3 + k_4 - \alpha_1).e^{-\alpha_1 t} + (\alpha_2 - k_3 - k_4).e^{-\alpha_2 t})] \otimes C_B(t) + f.C_B(t) \quad (2)$$

The ⊗ represents convolution, and

$$\alpha_1 = (k_2 + k_3 + k_4 - \sqrt{(k_2 + k_3 + k_4)^2 - 4k_2k_4})/2 \quad (3)$$

$$\alpha_2 = (k_2 + k_3 + k_4 + \sqrt{(k_2 + k_3 + k_4)^2 - 4k_2k_4})/2 \quad (4)$$

PTAC curve function $C_B(t)$ and TTAC curve function $C_T(t)$ are indicated as input function and output function respectively.

III. PKAIN: An Artificial Immune Network for Pharmacokinetics

In our previous work, an artificial immune network for parameter optimization of pharmacokinetics (PKAIN) is proposed and tested in several models [8]. The evolution of the PKAIN artificial immune network is described as follows [14]. In the first step, the artificial immune network is initialized by randomly generating network cells in solution space. Given a tracer kinetic model, parameter solution spaces such as low-bound and upper-bound of output parameters are defined. To solve FDG kinetic model which has been mentioned in Section II, parameters of $k_1 \sim k_4$ and f are required to be optimized simultaneously. One of the solutions of these parameters is encoded into a memory cell of the artificial immune network. For each cell m of $M^{(n)}$, clone selection with concurrent simplex mutation [9] step is done to generate new M^* population. Then m cell is replaced by the cell who is calculated with the highest affinity in the M^* . In the network suppression process, similar cells with lower affinity are deleted to maintain a relatively smaller network scale. The new generation $M^{(n+1)}$ of memory cells is generated. If the stop criterion is met, the evolution of memory cells stops. Finally, the memory cell with the highest affinity is decoded into an optimal parameter solution. Details of the PKAIN algorithm can be referred in the literature [10].

IV. Distributed Artificial Immune Network Based on Distributed Clone Selection with Concurrent Simplex Mutation

The main aim of the distributed PKAIN is to propose an efficient method to accelerate PKAIN algorithm executing speed. Recently, a parallelized artificial immune network for fuzzy clustering (PAINFCM) is designed and applied to fuzzy clustering [11]. In the PAINFCM algorithm [12], there were two models presented to improve efficiency of AIN for fuzzy clustering. One was the parallelized affinity calculation of the mutated antibodies. Based on the master-slave model, the AIN evolved in the master processor, and distributed affinity calculation of antibodies to slaves' processors. The other one is coarse-grained version of PAINFCM algorithm which was proposed to parallelize clone expansion.

For a traditional AIN, the clonal selection process of an artificial immune network is a computational implementation of the clonal selection principle [2] to solve optimization problems, emphasizing multimodal and combinatorial optimization [13]. The process of clonal selection is composed of clone expansion, affinity mutation and selection steps. Firstly, memory cells are sorted in their affinity values decadently. In the second step, the clone number of each memory cell is inversely proportional to its order, that is, memory cells with higher affinity will have more offspring. After clone expansion, antibodies of population undergo affinity maturation.

The Experiments show that the artificial immune network optimization of data analysis, with the increase in

the size of data processing algorithms to run slowly [1]. By the time complexity of algorithm analysis found, the algorithm of memory cell clones large population affinity calculation determined the rate of change in population variability situation is the main reason for the speed of algorithm execution. Therefore, this line of clone selection evolution, we can use independent methods of distributed computing will affect the time course of distribution to the various computing units, and each computing unit takes part of clonal selection tasks in the AIN, so that the distribution of the process of cloning can be completed faster.

For the PKAIN, it has a new clonal evolution called clonal selection with concurrent simplex mutation. There is a partition-based concurrent simplex method to be designed. That is after affinity mutation of traditional clonal selection process, antibodies are considered as a natural partition group to do simplex mutation. The number of cells of X is denoted as Nc , $Nc > L+1$. After executing concurrent simplex to X , there are $Nc - L$ number of new cells that have been updated. These new cells together compose the new generation of cells X . Then, the cell with the highest affinity is selected to substitute for the network cell m .

For the distributed PKAIN strategy, the only constraint of mutation is that mutation rate α is proportional to normalized affinity value. To solve this problem, normalized affinity should be distributed to processors. So, a new distributed PKAIN method with distributed clonal selection with concurrent simplex mutation is proposed. The procedure of the PKAIN with distributed clonal selection with concurrent simplex mutation is described by the following pseudocodes.

Initialize artificial immune network $M^{(0)}$.
While stopping criterion is not met do
Affinity calculation of each cell m in $M^{(n)}$, where n is the iteration number

Distribute p = 1…np $M^{(n)}(p)$ to processors

For each $m \in M^{(n)}(p)$ C= *clone_expension(m,*N_C*)*;

C^a = *affinity_mutation(*C);

C^s= *simplex_mutation*(C^a);

m^* = *selection(m,* C^s*)*;
END-Distribute and receive $M^*(p)$
$M = M^{(n)} \cup M^*$;
$M^{(n+1)}$= *network Suppression-Update(M)*;
END Do
Decode the m with the highest affinity into the optimal solution

V. EXPERIMENTS AND RESULTS

A. Data acquisition

Dynamic FDG studies were performed on four mice subjects. Each one have been recorded their sex and weigh. The experiment injected these mice with ^{18}F-FDG which performed at Siemens Invent Micro-the PET nuclear medicine for molecular imaging equipment in a period of time. For the purpose of this study, the data acquisition soft called Invent Acquisition workplace was implemented to dispose images from PET. The regions of interest (ROIs) selected for modeling with the proposed method were based on visual identification of their corresponding TAC.

B. MATLAB Distributed Computing Engine

MATLAB Distributed Computing Environment is a software platform in this study: one Intel Xeon server platform, four Lenovo Intel (R) Core (TM) 2.0 computers and network composition. Development software is the MATLAB R2009a, the MATLAB Distributed Computing Server 4.3, and the MATLAB Distributed Computing Toolbox 4.3. The MDCE is running with MATLAB distributed server and its toolbox program interface. It starts after the software installation services of distributed computing, programming for the distributed environment. The MDCE and distributed computing toolbox can be used to run on cluster computers for distributed and parallel MATLAB applications. Distributed algorithm tasks, including separate tasks, have no communication between them. They integrate the technical standards-based MPI functions in the MATLAB environment to support development of distributed applications. They can also create a distribution array of applications, support FOR loops and global array. This application does not require message passing, distributed computing or parallel through the implementation of the algorithm can improve the efficiency and save system development time. The client-job manager-workers architecture of the distributed computing configuration is described as follows.

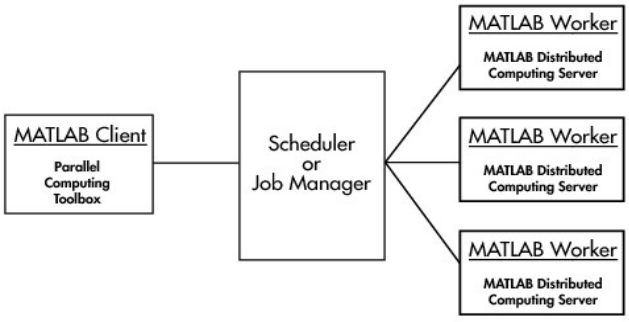

Figure 2. The client-job manager-workers architecture of the MDCE

According to the Fig.2, the MDCE enables us to coordinate and execute independent MATLAB operations simultaneously on a cluster of computers (various computing units), speeding up the execution of large MATLAB jobs. A job is some large operation that you need to perform in your MATLAB session. The MATLAB session in which the job and its tasks are defined is called the client session. Often, this is on the machine where you program MATLAB. The client uses MDCE server to

perform the definition of jobs and tasks. The job manager is the part of the server software that coordinates the execution of jobs and the evaluation of their tasks. The job manager distributes the tasks for evaluation to the server's individual MATLAB sessions called workers.

In the experiment, we use a master-slave distributed model. It is a model of coarse-grained parallel computing model. Master-slave model sets to host management of distributed PKAIN network encoding and cell population regeneration steps. As in the Fig.2, the client is the host management through the job-manager which divides the distribution of tasks to each worker. Then the slave workers take the responsibility for the clone selection and affinity calculation process. The job-manager is the MDCE scheduling program and deployed in distributed computing server. The distributed PKAIN clone selection evolution is the process of independent of sub-populations. Therefore, the end of the distribution of each sub-population of the affinity calculation results are brought together, MDCE provides a computing interface (PAFOR), can be achieved through distributed PKAIN clone selection strategy.

C. *Speed ratio analysis*

In order to evaluate the performance of distributed PKAIN algorithm, using Amdahl law namely absolute speed speedup ratio (index) is analyzed. Acceleration as formula calculation Eq.(5), where $T(1)$ means a processor serial algorithm in the execution time, $T(p)$ means p processors serial algorithm in the execution time.

$$SP(p) = \frac{T(1)}{T(p)} \tag{5}$$

For the cell clone selection constant impacts the speedup of the distributed PKAIN; the number of cloned cells of each memory cell is set as 50,100,200,400,800 respectively, for comparative analysis. Initialize artificial immune network parameters with the initial population size N = 40, mutation rate beta = 5, each iteration randomly generate new cell number d = 0.4, the number of iterations gen = 100, network suppression parameter ts = 0.1.

TABLE I. SPEEDUP OF DISTRIBUTED PKAIN WITH DIFFERENT THE NUMBER OF CLONED CELLS

Nc	CPU(processors)				
	P=2	***P=4***	***P=6***	***P=8***	***P=10***
50	1.08	2.01	4.46	5.46	6.14
100	1.91	3.45	4.36	5.01	5.90
200	1.77	3.36	4.29	5.80	6.64
400	1.68	3.34	5.62	6.92	7.00
800	2.24	3.13	5.48	6.83	7.67

Notes: Nc is the number of cloned cells, and p is the number of processors.

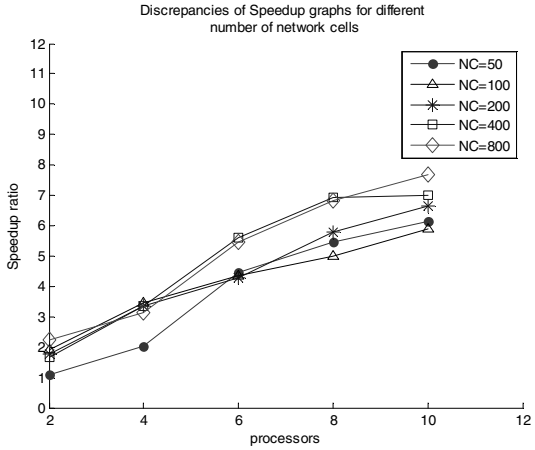

Figure 3. Discrepancies of Speedup graphs for different number of network clone cells

According to the above table and image, memory cells population become to influence the speedup ratio as an important factor with its numbers increased. As can be seen from Table I, this table gives to quantify the cloned population number compared with the increase of population and processor computing unit, the running time speedup goes up, and ultimately the number of species in 800 is that its running time is running single-core the 1/7.67 times. At this time population has reached a relatively high speed of operation (Fig.3). However, the distributed process as only the distribution of clone selection does not affect the accuracy of parameter optimization algorithms, so it can be shown to achieve the purposes that improved parameter optimization of tracer kinetics model to avoid the time-consuming.

VI. CONCLUSIONS

In this paper, the PKAIN method is to be accelerated to solve tracer kinetics modeling in a distributed way. The method to acquire distributed solutions is described in details and be implemented to optimization parameters for the compartment model of FDG tracer. While the accuracy results of the distributed algorithm kept, it can obtain higher speed. As the clone selection don't show any change of the algorithm efficiency. The distributed master-slave unit shows that distribution computing can save much more time in solving tracer kinetics problems. In addition, this algorithm also suitable for problems of other tracer kinetic models.

ACKNOWLEDGMENT

This research is supported by the Fundamental Research Funds for the Central Universities No.JUSRP10928 and Science and Technology Support of Wuxi City No. CSE01014.

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