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PANCREAS HORMONES- INSPIRED METHOD

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Abstract: This paper intends to formulate a new multi-objective inspired method, called Pancreas Hormones Method (PHM) for solving optimization problems. PHM is a population-based method, which based on biological nature of pancreas hormones in the maintenance of blood glucose level in the human body system. The adaptive blood glucose control system has provided useful alternatives and supplements to the types of optimization problems embodied in distributed systems. In this method, cell absorption of glucose is considered as a candidate solution; this happens when each cells' receptors in the human body bind with insulin granule, which allows utilizing glucose by a cell. The pancreas evaluates the fitness of all solutions by measure blood glucose level (BGL) in each iteration (secretion phases). Insulin granules (molecules) tend to target cells randomly and search for the optimal solutions which can get it by retard BGL to normal range. In each generation of the algorithm, the best solution is which can access the BGL to the balance point, whereas the other solutions are considered as a searcher of the search space. In this paper, PHM designed, and then it validated, tested on the bases of standard benchmarks and compared with the results of some successful algorithms. The results of PHM are promising.

Keywords: Pancreas hormones method (PHM); pancreas hormones algorithm (PHA); pancreas hormones; inspired algorithm, optimization.

1. INTRODUCTION

In daily life there exist many problems whose objective are to either maximize or minimize some value under some specific constraints such as load balancing in terms of maximizing quality of services (QoS) within cloud computing environment, and travelling salesman problem in case minimizing of trip route[1]. Modern optimization techniques start to demonstrate their power in dealing with hard optimization problems in robotics and automation: manufacturing cells formation, robot motion planning, worker scheduling, cell assignment, vehicle routing problem, assembly line balancing, shortest sequence planning, sensor placement, unmanned-aerial vehicles (UAV) communication relaying and multi-robot coordination [2]. These types of problems are optimization problems. In addition, there exist many problems which comes under the same category (NP-Hard). To get nearby optimal solution of these problems in polynomial time, the metaheuristics approaches are used[1]. Metaheuristics are algorithms which provides optimal solution by utilizing combination of exploration and exploitation. Metaheuristic algorithms are a higher-level heuristic (trial-and-error approach in generating new solutions) with the additional use of learning strategy. The vast majority of heuristic and metaheuristic algorithms have been derived from the behavior of biological systems and/or physical systems in nature. For example, particle swarm optimization was developed based on the swarm behavior of birds, insects and fish [3], [4], while simulated annealing was based on the annealing process of metals[5]. Hence it was the motivation of this method, in an attempt to find a general method to solve optimization problems inspired by precise and optimal system that stems from the biological nature of pancreas hormones in the maintenance of BGL in the body system. The pancreas in the human body work in multi-objective sides by increase or decrease the BGLs to keep BGLs in normal range (optimal solutions) by increase or decrease cells glucose levels (CGLs). In real it implicitly keeps cells glucose levels in normal range.

2. RELATED WORKS

PHM depended on two areas of studies, 1) optimization algorithms especially nature inspired algorithms, and 2) pancreatic hormones mechanism with its mathematical models, to try to imitate the pancreatic mechanism as algorithm for solving optimization problems.

2.1 Metaheuristics

Optimization algorithms are classified into deterministic, and non-deterministic or stochastic algorithms. The algorithm is considered deterministic when a given starting point lead to exactly the same sequence of solutions such as traditional algorithms. These algorithms depend on the mathematical nature of the problem. Weakness of these algorithms are local search, problem-specific, and the diversity of the obtained solutions can be very limited. On the other hand, stochastic algorithms are able to solve a diverse range of problems and more suitable to find optimal or near optimal solutions by using exploration (diversification, which allows the algorithm to search different regions in the design space and thus increases the probability of finding the true global optimality), and exploitation (search local regions more intensively). Most metaheuristic algorithms are nature-inspired algorithms which classified in stochastic class. These algorithms prove their success in most optimization problems [4], [6], [7]. Nature-inspired methods have been inspired by the behavior of biological, physical and chemical systems in nature, or behavior of animals or human body system. According to [6], [8] , the most successful algorithms in the nature inspired algorithms that classified under algorithms which inspired by animals and human body system's behavior, these algorithms include Genetic algorithm [9], Artificial neural network[10], Simulated Annealing[5], Tabu search[11], Artificial Immune System[12], Ant colony optimization[13], Particle Swarm Optimization[3], Harmony search[14], Artificial Bee Colony[15], Firefly Algorithm[16], Cuckoo Search[17]and Bat

Algorithm[18]…etc.These algorithms are among the most popular and best algorithms in solving optimization problems, and this is evidenced by the applications that used these algorithms and the high citations rates of these algorithms in the fields of research and application. Most of the algorithms in the literature can near to the optimal values for the test functions, but they need much work with high cost to find the exact optimal values. Therefore, a gap appears in the accuracy and convergence speed of the previous algorithms.

2.2 Pancreas Hormones Control System

PHM is a method that inspired by the nature of biological of complicated system in the human body. Although it's difficult to understand pancreas hormones mechanism and summarize it mathematically, but luckily there are many medical, biochemistry, bionic engineering and physiology studies which have studied the mechanism of glucose regulation in the human body to treat diabetics in the world. It is known that science has not found the exact mechanism of how this system works, but it is an ongoing challenge that keeps scientists working continually in order to improve their hypotheses as much as possible to help diabetics in the world. According to,[19] which explained the general mechanism of the (Glucose-Insulin-Glucagon) subsystems. It also, extracted the main equations among thirteen different study. Those studies crystallize the mechanism in the form of mathematical models which greatly facilitate understanding the mechanism of pancreas hormones and regulation mechanism. One of those models is Dalla Man model [20], which is the most model that is quoted and used to formulate PHM mathematically because, it was comprehensive mathematical model that presented (glucose- insulin) subsystem and, almost it was the closest model that could be useful in simply clarifying the functioning of the pancreatic mechanism. It's in turn combined from more than one study to represent the mechanism of the pancreas.

3. ORGANIZATION OF BLOOD GLUCOSE CONTROL SYSTEM

3.1 Behavior of Pancreas hormones

Glucose homeostasis is one of the most important phenomena in human body. Glucose (C6H12O6) is a monosaccharide used as the main source of energy in the body. It is oxidized in the cells to generate adenosine triphosphate (ATP) molecules which in turn provides energy to the cell [21]. Plasma glucose can originate exogenously from the ingestion of food and also endogenously from the liver by glycogenolysis [22]. This plasma passes through the cells, pancreas, and other organs in the body[21]. Glucose enters the cell by facilitated diffusion mechanisms, which represent an example of regulated mass exchange across the cell membrane. Specialized families of membrane proteins called GLUT (i.e., GLUcose) Transporters [10]observed in a large variety of cell types[23], actively operate the removal of free glucose from the interstitial spaces and transport it inside the cytoplasm, with distinct affinities and maximal transport rates [24]. The absorption of glucose in the cells determines the actual concentration of blood glucose [25]. The pancreas is one of the most important organs in glucose homeostasis. It continuously monitors blood glucose level that occurs when plasma glucose passes continuously through the pancreas's glucose transporter, the pancreas, in turn, secrete the appropriate hormone to regulate blood glucose level. All of this is controlled by integrated hormonal and enzymatic processes. The system comprises of many complicated sub-processes; whose erroneous activity usually leads to common diabetic diseases[25]. Human body system consist of various organs. Those organs have their own specific functions and play their roles in maintaining relevant biological activities in the body. To carry through its function, each organ needs a stable and adequate glucose supply from the blood. It is therefore important to keep the optimal blood glucose level [26]. The two main organs involved in the maintenance of glucose homeostasis are the pancreas and the liver. The role of the pancreas is that, releases the two most important hormones that control glucose homeostasis: insulin and glucagon. They produced in pancreatic-β cells, and pancreatic-α-cells respectively[27], [28], [24].When the blood glucose level is high β cells secrete insulin to help our cells in the process of glucose absorption. Whereas, α-cells secret Glucagon when blood glucose levels fall below normal. It acts as an antagonist of insulin by causing hepatic glucose output to rise[24], [27], [29]. The role of the liver is that, of a storage organ of excess blood glucose. When blood glucose levels are high, it takes up glucose and converts it into glycogen. When glucose levels are low, it releases glucose by either glycogenolysis or synthesizing new glucose (gluconeogenesis)[30]. Figure 1illustrate the mechanism of Glucose homeostasis.

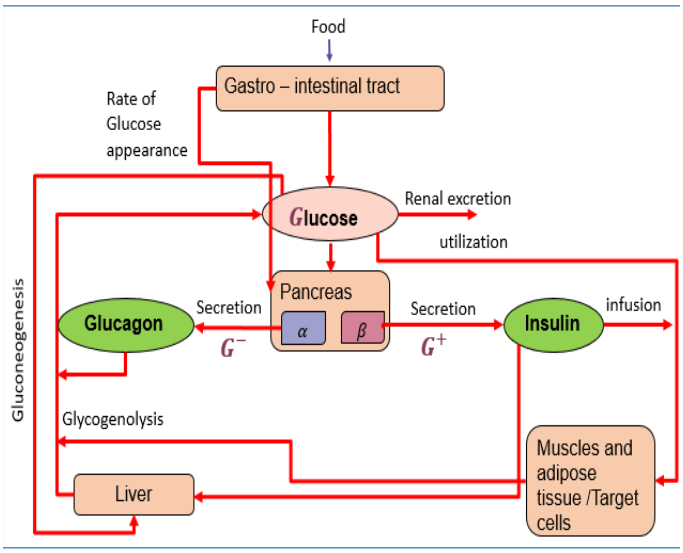

Figure 1: Mechanism of Regulation of Glucose level in human body

Plasma Glucose enter to Pancreas organs which can determine the rate of blood glucose, at high glucose concentration. This stimulate pancreatic β-cells to secrete insulin hormone. After plasma insulin is distributed to interstitial fluid, this activate glucose uptake by the target cells (as muscles) by binds insulin to cell-membrane receptors which allow to enter the glucose by target cell's transporter. whereas, at low glucose concentration, pancreatic α-cells secrete glucagon hormone which releases glucose by either glycogenolysis (re-converting stored glycogen from the liver) or synthesizing new glucose (gluconeogenesis). Excess proportion of the body is being removed from the body (Renal excretion)**[19]**.

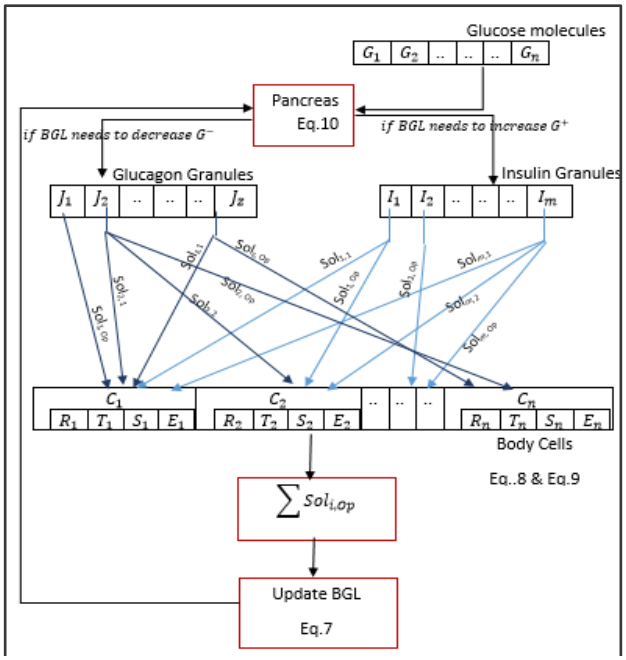

Figure 2: PHM's design

(plasma glucose (G) passes continuously through the pancreas's glucose transporter.Pancreas secrete the appropriate hormone.Insulin granules (I) tend randomly to target cells. Glucagon granules (J) tend randomly to target cells. The cell contains receptors (R) which work as a gate that doesn't allow to absorb glucose unless the cell need glucose for energy or storage. If the cell needs glucose, the target cell 's transporter (T) enters glucose from the interstitial spaces, then, transports it inside the cytoplasm with distinct affinities and maximal transport rates, while it outs glucose to blood when the cell has excess of the amount needed for the cell's energy production in case needing to balance BGL or CGLs.Transporters and receptors operate in succession. When the receptor is bound to the hormone (Insulin or Glycogen), the action of cell's transporters begins by absorbing or secreting glucose to and from the cell. The cell contains an amount of glucose (S) stored in excess of the amount needed for the cell's energy production (E).)

3.2 PHM Scenario with extracting its equations

The mechanism of the components of blood glucose control system that clarify in simple way in details in [19], which divide the mechanism to (glucose, insulin and glycogen) subsystems. This section demonstrates the scenario of the mechanism with clarification of the sequence of extracting equations that represent the work of the PHM which also summarize in Figure 2 that contains the design of PHM.

- The proportion of BGL is determined in the human body between 70-210, whereas, the normal balanced limit for the BGL is 80-110. As a first equation to compute BGL (G) at time $\boldsymbol{t+1}$, First, we consider ($\boldsymbol{\dot{G}^{t+1}}$) equals glucose masses in plasma $\boldsymbol{G_P}$at time t as follows equation:

$$\boldsymbol{\dot{G}^{t+1} = G^t{}_p} \text{ ……(Eq.1).}$$

- After a person has eaten a meal, it is transferred to the stomach and undergoes complicated digestive processes, as a result, the rate of G increased what is called *the rate of appearance* ($\boldsymbol{Ra}$) .since we are in this paper looking for a balancing process for the level of G in the blood , so we will track the meal after it converted into glucose and neglect previous digestive processes , $\boldsymbol{Ra}$ is added to **(***Eq.1***)**, so that, the equation becomes as follow:

$$\boldsymbol{\dot{G}^{t+1} = G^t{}_p + Ra^t} \text{…… (Eq.2).}$$

- Sometimes a person consumes a meal that consisting of high proportion of G such as honey, which leads to a significant increase in the proportion of G. This rise may be positive because it serves and supports the human body with energy, but everything has limited limits and weight. The human body takes its need of glucose until it reaches with its cells to the optimum extent, and the rest of it which is in excess of normal limit of BGL is dealt with by taking it out the body in excretion $\boldsymbol{E}$ process so the equation becomes as follows:

$$\boldsymbol{\dot{G}^{t+1} = G^t{}_p + Ra^t - E} \text{…… (Eq.3)}$$

- To access BGL to balancing point, there are two factors (hormones) that help in this, one of which is the process of increasing the level of blood glucose while the other is decreasing in order to effect the equilibrium process (in the next two points this will be details). (*Eq.7*) is the search equation for the best solution after neglecting two variables ($\boldsymbol{U_{ii}}$. $\boldsymbol{U_{id}}$) in *Eq.4* (Dalla Man equation[20]). There are cells that don't need insulin in the process of glucose utilization because they can't tolerate the delay resulting from responding to the need for glucose as brain cells (insulin independent utility $\boldsymbol{U_{ii}}$) , whereas, (insulin dependent utility $\boldsymbol{U_{id}}$) is the ratio that the blood needs to perform its work as blood cells which are considered also one type of body's cells which need glucose. This paper neglects these two variables but if the problem requires their existence, the equation will be (*Eq.4*),*where*: $\boldsymbol{U}$ is the amount of cells' glucose utility, and $G(c_i)^{t+1}$ in *(Eq.5)* is computed from *Eq.8* (Insulin hormone),

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$$\boldsymbol{\dot{G}^{t+1} = G^t{}_p + Ra^t - E + EGP - U_{ii} - U_{id}} \text{ −U… } \textit{(Eq.4)}$$

$$\boldsymbol{U = \sum_{i=1}^{n}(G(c_i)^{t+1} - G(c_i)^t)} \text{…… } \textit{(Eq.5)}$$

Endogenous glucose production ($\boldsymbol{EGP}$): is the amount of glucose that body's cells produce, $G(c_i)^{t+1}$ in *(Eq.6)* is computed from *Eq.9* (Glucagon hormone)

$$\boldsymbol{EGP = \sum_{i=1}^{n}(G(c_i)^t - G(c_i)^{t+1})} \text{…… } \textit{(Eq.6)}$$

$$\boldsymbol{\dot{G}^{t+1} = G^t{}_p + Ra^t - E + U - EGP} \text{…… } \textit{(Eq.7)}$$

- There are transporters and receptors in the body's cells. Transporters that help the cell in glucose absorption, the susceptibility of each cell type differs from others, some are able to absorb a very large amount of glucose (The liver), some require glucose in energy production (such as muscle cells), and some need glucose to convert it into fat (fat cells) etc. Also, cell contain receptors which work as a gate that doesn't allow to absorb glucose unless the cell need glucose for energy or storage. (In this paper we assume that each cell has one receptor just for simplicity).

Transporters and receptors operate in succession. When the receptor is bound to the hormone (**Insulin or Glycogen)**, the action of cell's transporters begins by absorbing or secreting glucose to and from the cell respectively.

- Insulin

Glucose uptake is activated once plasma insulin is distributed to interstitial fluid where it binds to cell-membrane receptors[21]. Insulin binding with cell's receptor is as an

indicator of the cell is needed for glucose either to produce energy[31], [32], (in this case, the cell has reached less than the minimum level of glucose in it). Or it has the necessary glucose for energy but 1) the blood glucose level is high and 2) the rest of cells that need glucose to not exceed the desired percentage which must shrink it from blood, so the cell absorbs glucose as a storage for future use, when it will need in energy producing at other times (between meals, sleeping, fasting, etc.). The target cell 's transporter enters glucose from the interstitial spaces and transports it inside the cytoplasm with distinct affinities ($affI_i$) and maximal transport rates (optimal solution –maximum value)[24]. Insulin secretion is done by biphasic secretion pattern[19], [22], [33] which is considered as iterations of mechanism for looking for the solutions which mechanism creates the first generation of insulin granules (First phase) leads to find global optimal solution (*Eq.7*). Whereas the others iterations (next generations of insulin granules (Second phase)) try to find the local optimal solution to retard synchronously BGL with CGLs to the optimal range *(Eq.10*). To access to the optimal solution, the objective function must get the minimum value of objective function whether the mechanism calls insulin or glycogen to increase or decrease BGL and CGLs. When insulin secretion phases are faded. At that time, the purpose of insulin secretion has been achieved which is to access to desired balancing by reducing BGL. In order to balance the BGL, this requires a decrease in the BGL, i.e. in other words, the cells absorb glucose, which decrease BGL by increase CGLs. That is, the amount of increase for all cells in the glucose level represents a solution in the mechanism in the process of creating a synchronous balance of blood and cell by retard them to their optimal solutions. This solution in PHM is represented and computed by *(Eq.8).* where $G(c_i)^{t+1}$ is the amount of G in cell i at time $t+1$,I_i is ability of bounding cell's receptor with insulin , it's value 0 or 1. 0 if the cell will not absorb glucose whereas it's value is 1 when the cell's receptor bind with insulin to allow the cell to absorb glucose and create one solution. The process of cell selection to generate new solution is done randomly by passing insulin granules in plasma after secrete them from pancreas to tend to the body's cells. Their passage in blood is therefore considered as passing through the cells of the body as an attempt to randomly connect insulin granule with the cells of the body to form an auxiliary solution to cause the balance process.

$$G(c_i)^{t+1} = G(c_i)^t + I_i * affI_i(G(c_{iOp})^t - G(c_i)^t) \ldots\ldots\ldots \quad (Eq.8)$$

$(affI_i)$ affinity of cell for absorbing glucose because each one of cells' type is different, the value of this variable is a distinct value between]0,1[specified by cells types (liver, muscles, fat, etc.) and $G(c_{iOp})^t$ is maximum optimal value of G in cell c_i

- Glucagon

Glycogen is the anti-insulin action hormone to induce equilibrium. It works if the BGL is low (fasting, between meals, sleep and exercises). It's secreted from the alpha cells in the form of granules with a biphasic secretion pattern until the balance is done. These granules tend to the glucose store in the liver to try to restore the equilibrium state of the BGL, but it may not suffice to induce the equilibrium process, so the granules are randomly go to the body's cells to extract the glucose from the cell's stores to create balance. In case, the cell contains an amount stored in excess of the amount needed for the cell's energy production process, it supports the blood in a specific percentage depending on the cell's susceptibility to loss ($affG_i$), the cell's glycogen receptor is bound to the glycogen granules and is allowed to be excreted through the cell's transporter into the blood.

$$G(c_i)^{t+1} = G(c_i)^t - J_i * affG_i * (G(c_i)^t - G(c_{Opmin})^t) \ldots\ldots\ldots\ldots\ldots \quad (Eq.9)$$

Where $G(c_{Opmin})^t$:is the maximum value to reach to the minimum that sufficient to produce energy, the range of values of $affG_i$ is between]0,1[,J_i is ability of bounding cell's receptor with glycogen , it's value 0 or 1. 0 if the cell doesn't able to excrete glucose whereas it's value is 1 when the cell's receptor bind with glycogen to allow the cell to excrete glucose and create one solution. As insulin work, in glycogen, the process of cell selection to generate new solution is done randomly by passing glycogen granules in plasma after secrete them from pancreas to tend to the body's cells. Their passage in blood is therefore considered as passing through the cells of the body as an attempt to randomly connect glycogen granule with the cells of the body to form an auxiliary solution to cause the balance process. $G(c_i)^{t+1}$ in *(Eq.9)* is the amount of G in cell i at time $t+1$ after construct of glycogen's solution .

- PHM objective function

$$\boldsymbol{Bobjf}(\dot{\boldsymbol{G}}) = (\boldsymbol{G^t - G_{optimal}}) - \sum_{\boldsymbol{i=1}}^{\boldsymbol{n}}(G\left(c_{i\,optimal}\right)^t - \textit{Gcit}) \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (Eq.10)$$

$\boldsymbol{Bobjf}(\boldsymbol{G})$:is the objective function of the mechanism which are comparing to access to the optimal solution for the blood and cells. This function for calculating fitness in a higher and lower solution, and since it works as a multi-objective function increase and decrease BGL. If the goal is decrease (by insulin hormone),the resulting value of $\boldsymbol{Bobjf}(\boldsymbol{G})$ will be a positive value whereas, when the goal is to increase (by glycogen hormone)),the resulting value of $\boldsymbol{Bobjf}(\boldsymbol{G})$ will be a negative value, but the best value for $\boldsymbol{Bobjf}(\boldsymbol{G})$ is at zero, which represents the arrival the mechanism to equilibrium with respect to blood and cells at the same time. Where $\boldsymbol{G_{optimal}}$ is the optimal value for blood's glucose, $G\left(c_{i\,optimal}\right)$ is the optimal value for cell's glucose(the algorithm considers the optimal is the access to the minimum for energy producing only not for energy and storage , we can adjust this according to the problem.).

3.3 Pancreas hormones algorithm

Begin
Objective function min or max $f(x)$. $x = (x_1 \ldots . x_d)^T$
Generate initial population of n *cells* $x_i (i = 1.2. \ldots . n)$
Set blood glucose level , BGL
Determine normal range of BGL, NBGL(80-110)
Sensing Glucose rate in the blood at any time point $t+1.G_i$
While $objectivefunction$ *not optimal*
Evaluate BGL and CGLs values by the objective function (Eq.10)
If $\boldsymbol{G^{t+1}} > NBGL$
Send signal to Pancreas (P) *to release insulin granules* (I).
Pancreatic-β cells Generate initial individuals of m *insulin granules* $S_j (j = 1.2. \ldots . m)$ *, then it secrete insulin granules to blood.*
insulin granules tend to x_1 *(liver cells) (storage of glucose)*

liver cells store Glucose in its store
Update BGL using (Eq. 4.7)
If $BGLstill > NBGL$
Insulin granules tend randomly to the target cellsx_i.
1.Evaluate x_i *excitation*
If x_i *excited for G*
Join S_j *to the receptor* $R_z \,.z = (z_1 \ldots . z_r)$
Assign G (glucose)to x_i*(for ATP or storage) using(Eq. 4.8)*
Else If x_i *inhibited for G*
Generate x_{i+1}*randomly and go to 1*
Else if $BGL < NBGL$
Send signal to (p) to release glucagon granules to blood
glucagon granules tend to x_i *(liver cells) (storage of glucose)*
liver cells Release Stored Glucose to blood
Update BGL using (Eq. 4.7)
If $BGLstill < NBGL$
glucagon granules tend randomly to the target cellsx_i
2.Evaluate cell x_i *excitation (of G secretion)*
If x_i *excited for G*
Join $Glucagon_j$ *to the receptor* $R_z \,.z = (z_1 \ldots . z_r)$
release G to blood using (Eq.9)
Else If x_i *inhibited for G*
Generate x_{i+1} *randomly and go to 2*
Update BGL using (Eq.7)
End

4 Implementation and Numerical Experiments

In the experiments, the solution representation can be either numbers or vectors depend on the problem, where we used numbers for simplicity. The PHM was implemented in Matlab, and tested on six diverse and well-known test functions, then compared with popular optimization algorithm to evaluate its performance. The number of iterations for the algorithm was set to 100 and the population size was set to 25.

In each iteration in PHM, an attempt is made to reach the equilibrium point for the level of glucose in the body's blood and cells, by passing them values to the objective function. When the equilibrium point (zero) is reached, the algorithm stops.

Figure 3showsthe results of algorithm for (20 Iteration) which satisfy the goal of algorithm in retard BGL and CGLs (Implicitly) to balancing point, while Figure 4shows the results for 100 iterations. The object function values (Bobjf(G)), represents a 100% success rate in finding the best solution and that worked by delivering blood and cells to the balance point, Figure 5represents how many times the algorithm has taken to reach to the optimal solution with standard deviation of its values STD=2.773686. PHM maximizes and minimizes BGL by Glycogen and insulin respectively, to reach to the best solution for BGL and CGLs. The results prove PHM efficiency in accuracy and convergence speed.

5 VALIDATION OF PHM BY STANDARD TEST FUNCTIONS

There are many benchmark test functions in literature [34], and they are designed to test the performance of optimization algorithms. Any new optimization algorithm should be validated and tested against these benchmark functions. In PHM simulations, we have used the following test functions.

1- Ackley

Ackley's function is subject to $-35 \leq x_i \leq 35$. The global minima is located at origin $x^* = (0.\cdots.0)$, $f_{Ackley}(x^*) = 0$.

$$f_{Ackley}(x) = 20 * (1 - e^{-0.02*(D^{-1}*\sum_{i=1}^{D} {x_i}^2)} - e^{-0.02*(D^{-1}*\sum_{i=1}^{D}\cos(2\pi x_i))} + e \quad \ldots\ldots\ldots (Eq.11)$$

PHM used f_{Ackley} as the objective function to validate its behavior to find the optimal solution, it success to find the optimal BGL and CGLs when it accessed to the global minima of f_{Ackley}.It could find the optimal solution after ≈5 iterations.The landscape of this function is shown in Figure 7. This global optimum can easily be found using PHM, and the results are shown in Figure 6, Which represents how times PHM needed to find optimal value of Ackley's function in 100 iterations, where the final values of the BGLs are also represent the optimal value of f_{Ackley} is founded.

2- **De Jong**

De Jong's function is essentially a sphere functionwhose global minimum $f_{DeJong\ *} = 0$ occurs at $* = (0.0.\ldots.0)$, $d$is the dimension.$x_i \epsilon$[-5.12,5.12].

$$f_{DeJong}(x) = \sum_{i=1}^{d} {x_i}^2 \ldots\ldots\ldots\ldots (Eq.12)$$

When PHM is evaluated by f_{DeJong} , it could find the optimal solution after ≈ 3 iterations (average of No. of Iterations to find the optima in (100 runs)= 3.24) as shown in Figure 8.

3- Griewank

Griewank is subject to $-600 \leq x_i \leq 600$. The global minima is located at $x = f_{Griewank}(0.\cdots.0). f_{Griewank}(x_*) = 0$.

$$f_{\text{Griewank}}(x) = \sum_{i=1}^{d} \frac{{x_i}^2}{4000} - \prod_{i=1}^{d} cos\left(\frac{x_i}{\sqrt{i}}\right) + 1. \ (Eq.\ 13)$$

When PHM is evaluated by $f_{\mathbf{Griewank}}$, it could find the optimal solution after ≈ 13 iterations (average of No.of Iterations to find the optima in (100 runs)= 12.62) as shown in Figure 9.

4- Rastrigin

$$f_{\boldsymbol{Rastrigin}}(x) = {x_1}^2 + {x_2}^2 - 10\cos(2\pi x_1) - 10\cos(2\pi x_2) + 20 \ldots\ldots\ldots (Eq.\ 14)$$

The global minimum of $f_{\boldsymbol{Rastrigin}_*} = 0$ at (0,0). $x_i \epsilon$[-5.12,5.12] The best among the comparison algorithms to find the optimal value for $f_{\text{Rastrigin}}$ could find the optimal solution after ≈ 50 iterations. Whereas, PHM is evaluated by $f_{\text{Rastrigin}}$, it could find the optimal solution after ≈ 4 iterations (average of No. of Iterations to find the optima in (100 runs)= 4.47) as shown in Figure 10.

5- Rosenbrock

$f_{Rosenbrock}(x) = \sum_{i=1}^{d-1}[100(x_{i+1} - {x_i}^2)^2 + (x_i - 1)^2]$. ……. (Eq. 15)

$subjectto - 30 \leq x_i \leq 30. The global minima is located at x_* = f_{Rosenbrock}(1.\ldots 1). f_{Rosenbrock}(x_*) = 0$

This global optimum also can easily be found using PHM, and the results are shown in Figure 11. Which represents how times

PHM needed to find optimal value of Rosenbrock's function. The best among the comparison algorithms was CS to find the optimal value for $f_{Rosenbrock}$, it could find the optimal solution after ≈ 65 iterations then KA which could find the optima after≈ 64 iterations. Whereas, PHM is evaluated by $f_{Rosenbrock}$, it could find the optimal solution after ≈ 5 iterations (average of No. of Iterations to find the optima in (100 runs)= 5.2).

6- Zakharov

The global minima is located at$x_* = f_{Zakharov}(0.\cdots . 0. f(x*) = 0, xi\epsilon[-5.10]$

$f_{Zakharov}(x) = \sum_{i=1}^{n} {x_i}^2 + \frac{1}{2}(\sum_{i=1}^{n} ix_i)^2 + \frac{1}{2}(\sum_{i=1}^{n} ix_i)^4$ ..... **(***Eq.16)*

In each iteration in PHM, an attempt is made to reach the equilibrium point for the level of glucose in the body's blood and cells, by passing them values to the objective function. When the equilibrium point (zero) is reached, the algorithm stops.

Figure 3 shows the results of algorithm for (20 Iteration) which satisfy the goal of algorithm in retard BGL and CGLs(Implicitly) to balancing point, while Figure 4 shows the results for 100 iterations which contains in glucose values as random values entered into the algorithm to manipulated them, and the output values of BGLs, which are all at 100% optimal values, the object function values ($Bobjf(G)$), represent a 100% success rate in finding the best solution and that worked by delivering blood and cells to the balance point, Figure 5represents how many times the algorithm has taken to reach to the optimal solution with standard deviation of its values STD=2.773686 for 100 iterations. PHM maximizes and minimizes BGL by Glycogen and insulin respectively, to reach to the best solution for BGL and CGLs.

The results of PHM are compared with the available results of the most popular and successful optimization algorithms in literature to compare their performance, speed and robustness. The results are compared with genetic algorithm (GA), particle swarm optimization (PSO), cuckoo search(CS), bat algorithm (BA), firefly algorithm (FA) and kidney algorithm (KA), that are previously reported in [17], [35], [36] to evaluate the PHM performance in finding the optima for 5 of the test functions which used in the PHM's validation and evaluation phase. The resultsof this comparison is summarized in Figure 12which prove the successful of PHMwithhigh performance to find the optimal value for the target test functions in professional time compared with other popular and success algorithms. Most of the algorithms can near to the optimal value for the test functions whereas, PHM is implemented and can easily find the exact global optimal values of the 5 test functions that used to validate this method.

Table 1shows summary of PHM comparison with the available results of the most popular and successful optimization algorithms GA, PSO and FPA ,which are previously reported in [37],while Table 2 shows summary of PHM comparison with the available results of another optimization algorithms Firefly, CS, and ACCS ,which are previously reported in [38] to prove the accuracy of the PHM.The statistical analysis proved the ability of the PHM to find the optimal solution with a high speed and less function evaluations compared to other algorithms on six test functions.

Table 1: Comparison of algorithms performance and accuracy: mean values.

Algorithm / Functions	GA	PSO	FPA	PHM
Ackley	8.29e-9	7.12e-12	5.09e-12	0
Sphere	6.61e-15	1.18e-24	2.47e-26	0
Griewank	5.72e-9	4.69e-9	1.37e-11	0
Rastrigin	2.93e-6	3.44e-6	4.52e-7	0
Rosenbrock	8.97e-6	8.21e-8	6.19e-8	0
Zakharov	8.77e-4	1.58e-4	9.53e-5	0

Table 2 : Global optimization results of benchmark functions.

Algorithm / Functions	Firefly	CS	ACCS	PHM
Ackley	1.83652	0.33521	1.0066×10^{-35}	0.00
Sphere	2.388×10^{-7}	4.634	1.211×10^{-49}	0.00
Griewank	0.334255	1.005346	0.006555	0.00
Rastrigin	114.022	83.4389	1.88747	0.00
Rosenbrock	147.232	78.252	22.6195	0.00

6 CONCLUSION

This paper proposed a new method that called pancreas hormones method (PHM)for solving the optimization problem. This method imitated the biological of the pancreas hormone system in the human body system. In this simulation, the solutions in the population are produced by insulin and glycogen granules and evaluated based on their objective functions. Secretion steps are applied for search in the area to find the optimal solution of BGL which also represents the optimal for CGLs, that occurs after all graduals finished search process. Summation of the solutions that produced by each secretion phase in each iteration that represent one solution in the algorithm that is evaluated by pancreas (objective

function) to access to the optimal level. Glucose absorption or secretion represents the solution in the PHM. Some solutions that have already had chance of absorbing but cannot be assigned to any cell because the BGLexceeds the limit of glucose range so, they are excreted. The implementation of the algorithm and its results for six standard test functions showed that the algorithm is effective and its performance is better on the six test functions when compared with the most popular and successful algorithms in literature. PHM is able to find the global optimum with less function evaluations compared to other algorithms. The statistical analysis proved the ability of the algorithm as it had fewer function evaluations compared to other algorithms.

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APPENDICES

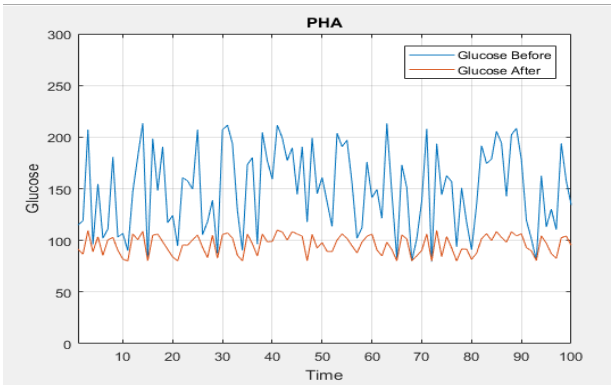

Figure 3:Inputs and outputs values of glucose in PHM (20 Iterations).

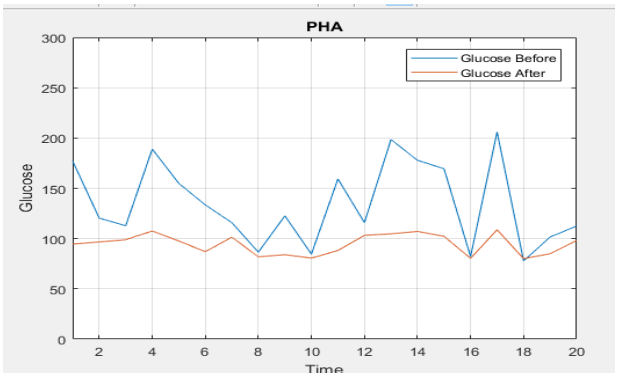

Figure 4: Inputs and outputs values of glucose in PHM (100 Iteration).

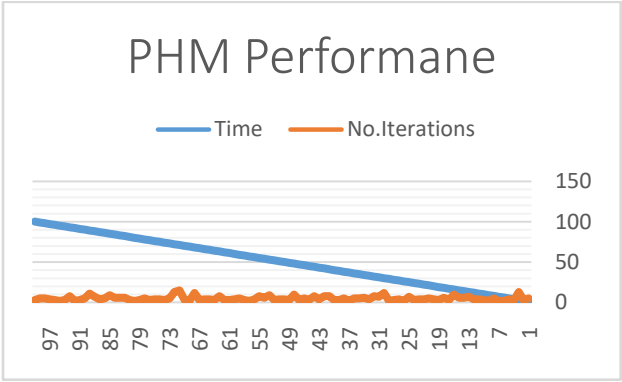

Figure 5: PHM performance.

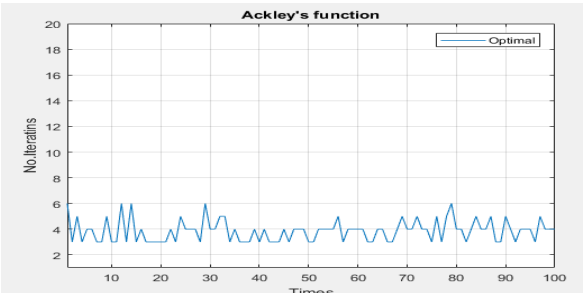

Figure 6: Ackley's function implementation.

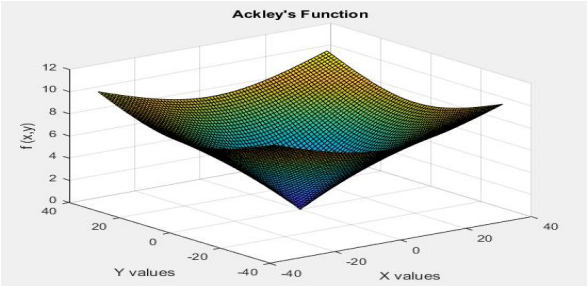

Figure 7: landscaped of Ackley's function.

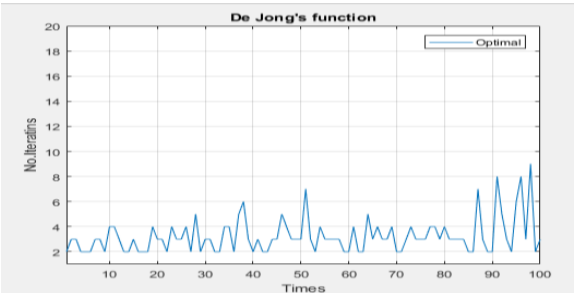

Figure 8: De Jong's function implementation.

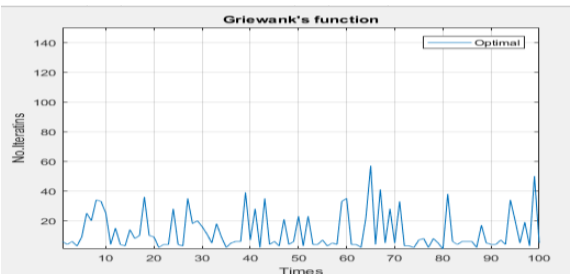

Figure 9: Griewank's function implementation.

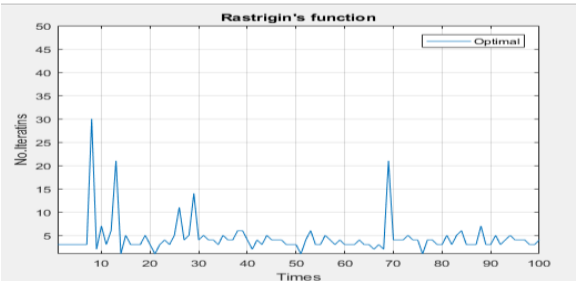

Figure 10:Rastrigin's function implementation.

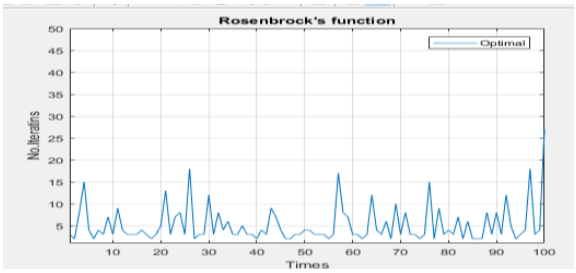

Figure 11: Rosenbrock's function implementation.

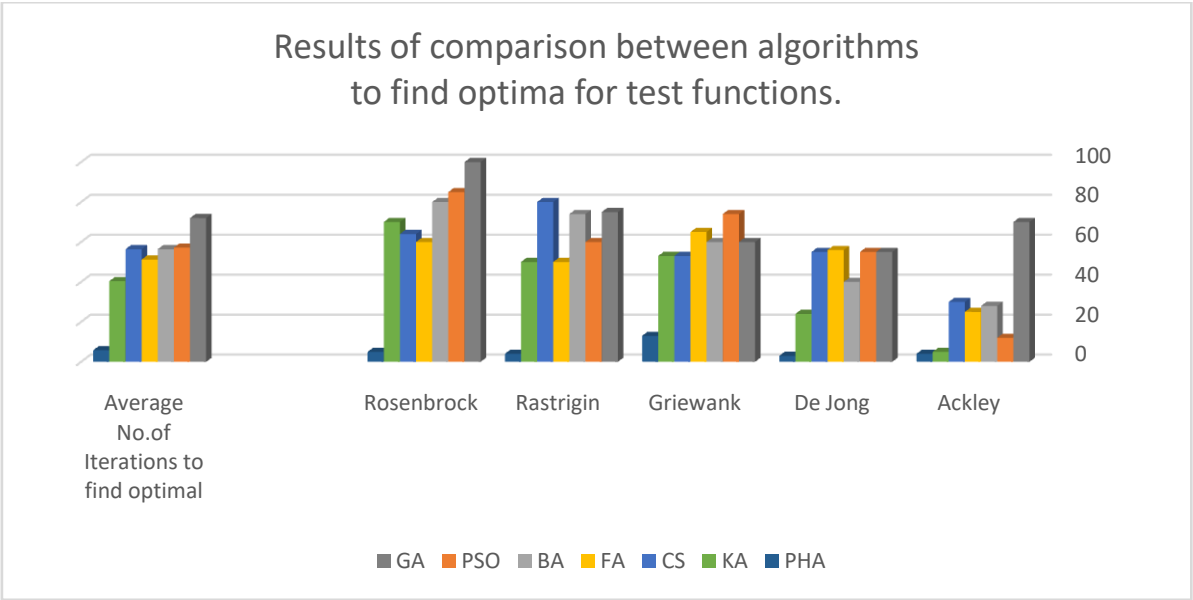

Figure 12: Results of validation by using test function.