Abstract—As nanotechnology advances, the use of nanotechnology for medical purposes in the field of nanomedicine seems more promising; the rise of nanorobots for medical diagnostics and treatments could be arriving in the near future. This study proposes a swarm intelligence based control mechanism for swarm nanorobots that operate as artificial platelets to search for wounds. The canonical particle swarm optimization algorithm is employed in this study. A simulation in the circulatory system is constructed and used for demonstrating the movement of nanorobots with essential characteristics to examine the performance of proposed control mechanism. The effects of three nanorobot capabilities including their perception range, maximum velocity and respond time are investigated. The results show that canonical particle swarm optimization can be used to control the early version nanorobots with simple behaviors and actions.

Keywords—Artificial platelets, canonical particle swarm optimization, nanomedicine, nanorobot, swarm intelligence.

I. INTRODUCTION

The advancement of medical technology improves the effectiveness of diagnosis, monitoring and treatment. Nevertheless, some diseases are difficult to diagnose at the early state and some treatments i.e. surgery and medicine also have risks and side effects to other healthy cells. Since the development of nanotechnology has been continuously progressed, nano-scale robots (or nanorobots) that are small enough to move along blood vessels could be used to treat targeted abnormal cells i.e. cancer cells and infected cells directly to enhance medical efficacy with minimal risks and side effects.

The idea of nanotechnology was introduced by Richard P. Feynman in 1959 [1]. Researchers have been applying and developing nanotechnology for various purposes, for example, improving the properties of materials in material science, reducing the size of electronic devices in electrical engineering and, using biological molecular as sensor to detect other low concentration molecules in biological science [2]. In 1986, K. Eric Drexler [3] introduced the idea that cooperative small robots could be injected into human body and could manipulate substances or build simple structures on molecular scales with robotic arms. Since then, research for medical applications has been conducted; for example, Robert A. Freitas Jr. designed medical nanorobots i.e. respirocytes [4], which are artificial mechanical red blood cells transferring oxygen and carbon dioxide between respirocytes and body tissues, microbovores [5], which are artificial mechanical white blood cells identifying and digesting unwanted and foreign substances, and clottocytes [6], artificial platelets assisting in primary hemostasis to stop bleeding by releasing their mesh to the site of damaged blood vessels. In addition, Cavalcanti and Freitas [7] developed a simulation of nanorobots to transport nutrition to organ inlets. Because nanorobots are not yet realized, the simulation of nanorobots will be beneficial to identify the essential characteristics and to investigate the effectiveness of control techniques; the findings can serve as guidelines for developing nanorobots in the future [8]. However, the simulation of nanorobots should be as realistic as possible so that the findings can be truly beneficial for the realization of nanorobots. At the early stage of nanorobots, their characteristics and capabilities may be limited by their sizes. They may be able to exhibit only simple behaviors. Each nanorobot will connect to each other to form a structure without centralized control (self-assembly). Self-assembling processes are commonly found in nature e.g. lipids self-assembling into membranes [9]. Moreover, collaborative behaviors among groups of individuals that enable self-assembly can be discovered in social animals such as birds, ants, fish and termites. Such swarm intelligence can be modeled and applied for solving optimization problems [10]-[11]. Swarm intelligence techniques are plausible to apply for controlling the nanorobots. The aim of this study is to investigate the possibility of using a swarm intelligence technique to control a swarm system of nanorobots with only essential characteristics to operate as artificial platelets in circulatory system for seeking the wound. The primary hemostasis is chosen in this study because the task is an example of self-assembly in nature and simple enough for the early stage nanorobots. Section II describes the physiological information of platelets and their role in primary hemostasis. The characteristics of swarm intelligence techniques that are suitable for controlling nanorobots are discussed in section III. In section IV, the design of nanorobots and their control mechanism are described. The experimental design for this study is discussed in section V. The result and discussion are included in section VI. Finally, the study is concluded in section VII.

II. PLATELETS

Platelets (thrombocytes) are anuclear blood cells, which are about 2-4 µm in diameter and can circulate in the system for 7-10 days. They are discoid-shaped in resting state and irregular-shaped in activated state. Platelets are derived from fragmentation of precursor megakaryocytes, which are cells in the bone marrow. The normal platelet count is 150,000-

P. Boonrong is with the Biological Engineering Program, King Mongkut's University of Technology Thonburi (KMUTT), Bangkok, Thailand (e-mail: pinfa21@gmail.com).

B. Kaewkamnerdpong is with the Biological Engineering Program, King Mongkut’s University of Technology Thonburi (KMUTT), Bangkok, Thailand (e-mail: boonserm.kae@kmutt.ac.th).
400,000 per micro-liter of blood [12]. When a blood vessel wall is injured, platelets adhere to the exposed collagen and von Willebrand factor in the wall via the receptors on the platelet membrane. Due to the adhesion, the platelets become activated; then, their shapes are changed, their receptors are activated, and the contents of their granules are released to stimulate neighboring platelets. Platelet aggregation is mediated by the interaction of fibrinogen. The above process is the first response in human body to stop bleeding, known as primary hemostasis [12]. However, in some patients blood clots are formed irregularly. The abnormality or diseases of platelets are characterized in terms of disorders in the number of platelets (thrombocytopenias) and their functions [13]-[14].

Treatments of these diseases are medicines (corticosteroids), platelet transfusions or splenectomy [14]. Nevertheless, these treatments have side effects; for example, corticosteroids could affect hormone secretions, blood or platelet transfusions could damage lung, and some people may have allergic reactions. Splenectomy will reduce the production of antibodies, so the patients gain higher risk to get infections [12]. To treat patients with platelet diseases, the medical nanorobots, clottocytes, are designed to carry fiber mesh and to release their mesh over the injury in order to accelerate the clotting process [6]. However, based on current development in nanotechnology, clottocytes may be too complex to be realized in the near future. In this study, nanorobots are models of an early-version of nanorobots that might be simpler than the complex version in [6] but still effective; in this study, nanorobots are regarded as biocompatible molecules self-assembling at the wound site to form a temporary plug to trap blood components and let the hemostasis process continue the formation of the clot.

III. Swarm Intelligence

Swarm intelligence techniques are artificial intelligence algorithms inspired by collective intelligence arising from the collaborative behaviors of social animals such as ants, termites, bees, flocks of birds and schools of fish [10]-[11]. These social animals require no leader; in other words, they work without a centralized control. Their collaborative behaviors emerge from relatively simple actions, interactions among the individuals in the group, and interactions with their environment. Although each individual may not be intelligent, together they perform complex collaborative behaviors such as foraging and nest building. Swarm intelligence techniques can be used to solve complex optimization problems [11]. Behaviors of nanorobots in this study are similar to social animals. Therefore, swarm intelligence could be used to control a swarm system of nanorobots. There are three main types of swarm intelligence techniques: ant colony optimization (ACO), artificial bee colony (ABC) and particle swarm optimization (PSO) [11]. ACO is inspired by ant foraging behavior. Ants communicate to other ants indirectly through pheromone trails deposited along their path; the deposition and evaporation of pheromone concentration enable ants to find the shortest path between their nest and the best food source. The first algorithmic model of ant foraging behavior was developed by Dorigo in 1992 [15]. ACO has been used to solve the optimization problems such as travelling salesman problem (TSP) [16] and network routing [11]. Moreover, ACO has been employed in physical applications such as robotics; pheromone robots or pherobots use infrared transceivers to send and receive information of virtual pheromone among neighbors [17]. Pherobots determine pheromone intensity from the signal and the estimated distance from the sender and, then, transmit the updated pheromone intensity to their neighbors. This method can roughly simulate pheromone detection and pheromone concentration gradient. Nevertheless, the transmission of such virtual pheromone information may not be plausible in the early stage of nanorobots. ABC inspired by the foraging behavior of honey bees was proposed by Karaboga in 2005 [18]. In ABC, after employed bees found food sources (feasible solutions), they fly back to the hive and dance to share the information on the quality of nectar from their food source (the fitness of solution) to onlooker bees. Each onlooker bee selects one of the food sources depending on the obtained information to exploit the food source. The recruitment of onlooker bees to a food source can lead to the best food source (optimal solution). If an employed bee cannot find a better food source for a predefined number of iterations, it will desert the food source and becomes scout bee randomly looking for new one. The local optimal solution can be avoided by scout bees. Nevertheless, the information sharing among bees at their hive may be difficult for the simple-version nanorobots in dynamic environment such as bloodstream. PSO is an optimization algorithm inspired by bird flocking and fish schooling. PSO was developed by Kennedy and Eberhart in 1995 [19]. The PSO algorithm regulates the movement of a swarm of particles. Each particle represents a potential solution to the problem. It moves around the problem search space to find an optimal or good enough solution. Each particle can communicate with other individuals to exchange information and modify the velocity according to its experience and the experience of its neighbors depending on the social network structure; hence, finding a good solution is influenced by both the experience of each particle and that of neighboring particles. The advantage of PSO is that there are very few parameters to adjust and it uses less memory. PSO seems plausible to apply in nanorobot coordination control or other physical applications.

IV. Nanorobots

A. Nanorobot Design and Characteristics

The early-stage nanorobots may potentially be simple entities and exhibit only simple behaviors similar to social insects in nature [20]. The essential characteristics of each nanorobot can be considered from the macroscale robots. Hence, nanorobots that act as artificial platelets and assemble themselves to repair the damaged blood vessel must be able to...
move around the environment,
interact with other nanorobots and its environment,
carry defined characteristics for the assembly task,
connect to another nanorobot at a specific area, and
operate inside human body with biocompatibility.

Similar to macroscale robots, nanorobots will require the features including actuator, signal generator and sensor, programmability and connection to other nanorobots for self-assembly. In this study, each nanorobot is sphere in shape similar to clutchocyte. The size of nanorobots in this study is 2 µm in diameter similar to the natural platelet [12] and clutchocyte.

For physical application, each nanorobot is limited to interact with others and its environment within a defined perception range.

B. Nanorobot control

The processes of nanorobots are designed according to the primary hemostasis. The nanorobots move along blood vessels to search for the wound, adhere to the damaged site and, then, release the signal to activate others. Finally, nanorobots connect with others to form a mass at the target site.

According to the tasks of artificial platelets, nanorobot control can be divided into 2 parts: seeking the wound and forming into the structure. This study only focuses on the seeking part to investigate the possibility of using swarm intelligence techniques for controlling a swarm of nanorobots. In this study, the canonical PSO algorithm developed by Clerc and Kennedy [21] was employed for that it is most suitable for this application as discussed in section III. In canonical PSO, the constriction coefficient factor that controls the exploration versus exploitation trade-off is introduced to ensure the convergence of PSO [21].

Each nanorobot (particle) moves in three-dimensional model of a blood vessel. The performance of each nanorobot is the distance between the nanorobot and the wound. The velocity of nanorobot obtained from the velocity update according to canonical PSO. Each nanorobot has signaling and sensing units with limited perception range and taking the average position of all neighboring position as the local best position.

As nanorobots have not been realized yet, the use of canonical PSO to control a swarm system of nanorobots with essential characteristics must be investigated in a simulation system. A simulation of a nanorobot system operating in circulatory system model is implemented using MATLAB.

A. Circulatory System Model

In this study, the environment of nanorobots is the bloodstream in a blood vessel. A blood vessel in human circulatory system and the blood flow are modeled. Blood flow in the model is in pulsatile motion according to the change of pressure inside blood vessels as the heart pumps. To simplify the model, a blood vessel is represented by a segment of a cylindrical tube in a closed system; the ends of the tube are connected as a torus. The process of fluid passing through membranes in blood vessels, called osmosis, is disregarded. In addition, it is assumed that the blood can be treated as Newtonian fluid whose viscosity remains constant for a changing range of shear rate and shear stress.

In this study, the model simulates blood flow in an arteriole which is a small blood vessel. Blood flow in an arteriole exhibit as laminar flow. The parameter values of the vessel model are shown in Table II. These parameters are set according to the physiological information in [12]-[22]. The vessel length ranges from -250 to 250. The wound is modeled as a cylinder with the radius of 5 µm, and the center of the wound is located at [15, 270, 0] in cylindrical coordinates (r, θ, z). The layer of endothelium cells which attracts nanorobots in an arteriole is assumed as 3 µm in thickness.

TABLE II
THE PARAMETER VALUES OF AN ARTERIOLE AS A RIGID TUBE WITH PULSATILE FLOW MODEL [12]-[22]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vessel thickness</td>
<td>20 µm</td>
</tr>
<tr>
<td>Vessel outer radius</td>
<td>35 µm</td>
</tr>
<tr>
<td>Vessel inner radius</td>
<td>15 µm</td>
</tr>
<tr>
<td>Vessel length</td>
<td>500 µm</td>
</tr>
<tr>
<td>Endothelium layer</td>
<td>3 µm</td>
</tr>
<tr>
<td>Blood density (ρ)</td>
<td>1050 kg/m³</td>
</tr>
<tr>
<td>Dynamic viscosity (µ)</td>
<td>0.00356 Pa.s</td>
</tr>
<tr>
<td>Kinematic viscosity (ν)</td>
<td>3.302 × 10⁻⁶ m²/s</td>
</tr>
<tr>
<td>Pressure gradient</td>
<td>-20000-4000(cosω)</td>
</tr>
</tbody>
</table>

B. Nanorobot Control

To investigate the performance of nanorobot swarm with
essential characteristics, the effectiveness and efficiency of nanorobots controlled by the canonical PSO algorithm is compared with those using random movement. The speed to achieve the goal is used as the indicator for the performance of nanorobots in finding the wound. There are three parameters affecting the effectiveness and efficiency of nanorobot control: the perception range, maximum velocity (VMAX) and time step size. Perception range is the area that a nanorobot can interact with other individuals and its environment; it depends on the capability of signaling and sensing units in nanorobots. VMAX is the maximum velocity allowed for nanorobots to travel. In real nanorobots, this value is defined by the actuator ability. The nanorobot can move faster when VMAX value is larger. However, how fast a nanorobot can travel is also dependent on the time step size, which is according to the nanorobot ability to respond to the control mechanism. In this study, the effects of all three parameters are investigated. The parameter settings for the experiments for the swarm system with canonical PSO control mechanism and random movement mechanism are described as follows:

1) The effect of different perception ranges: the experiment with five different perception ranges (3, 4, 5, 6 and 7 µm) is conducted while VMAX is fixed at 190.50 µm/s, and the time step size is set as 100.

2) The effect of various maximum velocities: the experiment with five levels of maximum velocity (47.62, 95.25, 190.50, 381.00 and 762.00 µm/s) is conducted when the perception range is set as 5 µm, and the time step size is fixed at 100.

3) The effect of different time step settings: the experiment with three different number of time step per second (100, 500 and 1000) is performed when the perception range is 5 µm, and VMAX is fixed at 190.50 µm/s.

The number of nanorobots is fixed at 142 nanorobots in all experiments; the number of nanorobots is set according to normal platelet concentration proportional to the size of blood vessel in this simulation model. Each experiment is run ten times for obtaining reliable data. The size of nanorobots is 2.0 µm in diameter similar to the clottocytes by Freitas [6] and natural platelets [12]. The position of each nanorobot is initially set to a random location in blood vessel model. The velocity of each nanorobot is randomly initialized between −VMAX and +VMAX. At initialization, the personal best position of each nanorobot is set to its initial position. The systems terminate when they reach the maximum iteration of 10,000 or when 28 nanorobots (the approximate number of nanorobots required to form into a mass to fill the wound site) find the wound (the distance between the nanorobot locations and the wound must be less than 0.5e-6 µm).

VI. RESULT AND DISCUSSION

For different parameter settings, the nanorobot swarm can find the wound at various numbers of iterations as illustrated in Fig. 1. From the result, the different perception range demonstrated the same levels of iterations required for seeking the wound site. In terms of varying time step size, the greater the time step size per second, the faster the response ability. It is because the faster response brings about a better adjustment of their position to the situation. For the effect of maximum velocity which limits the nanorobot movement step size, nanorobots spent more time to find the wound when VMAX is increased; it may be because the greater VMAX allows nanorobots to move with a larger step and could lead to more collision to the vessel wall or could overstep the wound.

Compared to the system with random movement, the results from the system with canonical PSO based control mechanism showed quite similar trends, but the nanorobot swarm with random movement can reach the wound faster in some cases. PSO relies on its own experience and the exchange of information among neighbors to influence the particle movement. In this study, nanorobots have no knowledge of their current locations in the environment and they cannot share their information with their neighbors. Apart from the
limitation on the exchange of information among nanorobots, other influences from the dynamic environment, i.e. blood flow in the vessel, also contribute in the unfavorable results. When the canonical PSO algorithm calculates for new movement, nanorobots cannot travel to the desired position due to the external influence from the blood flow. Nevertheless, the nanorobots with defined essential characteristics cannot acknowledge the changes in their movement caused by the blood flow. The information from the nanorobots’ personal best position which is calculated from accumulating their movement from the previous personal best position can be misleading. Hence, the nanorobots could no longer move toward the intended location. Moreover, as the local best position is the average of randomly selected neighboring location, the resulting local best position is merely a random position within the perception range. As the simulation advances, the movement of nanorobots becomes more like random movement no matter how large the perception range is. Although the nanorobots with random movement can adequately accomplish this simple task, the random movement approach may not be effective for more complex self-assembly tasks. Nanorobots may need additional characteristics to the defined essential characteristics in section IV. In natural primary hemostasis, the adhered platelets at the wound release chemical to induce neighboring platelets to aggregate around the wound site [12]. Hence, the ability to generate signal attracting other nanorobots and to sense the attraction signal may be essential for effective performing as artificial platelets. For medical nanorobots operating in the bloodstream, the ability to sense the external changes in the environment that could affect the nanorobot movement may also be beneficial to improve the nanorobot performance. An example for fluid velocity sensing in nature is the lateral line in fish [23]. The lateral line on the surface of fish is a sensing organ consisting of a set of neuromasts. Each neuromast contains a group of mechanosensory hair cells which detect fluid movement. Fish use their lateral line system to locate preys and to avoid predators. In addition, there are many various examples of highly sensitive hairs in several animals such as crickets, spiders and scorpions. These lateral-line or highly sensitive hairs could be used as a model of blood velocity sensor. To investigate the need of attraction signaling and sensing units and blood velocity sensor for nanorobots to operate as artificial platelets, additional experiments on the swarm system using canonical PSO are conducted. In Fig. 2, the nanorobots with attraction signaling and sensing unit and those with blood velocity sensing unit can outperform the nanorobots with random movement in some cases. In terms of the effect of perception range, the performance of nanorobots with attraction signaling and sensing unit is similar to the random movement approach; the nanorobots with blood velocity sensing unit can reach the wound with less number of iterations for all varying perception range values. Moreover, the nanorobots with blood velocity sensing unit perform better than other systems in the case of the number of time step per second is at 100.

For the effect of maximum velocity, both the system with attraction signaling and sensing unit and the system with blood velocity sensing abilities allow nanorobots to perform better than random movement when the maximum velocity is less than 190.50 µm/s. With the knowledge external influence around nanorobots, each nanorobot obtains correct information for its personal best position so it can move to the optimal position according to the canonical PSO algorithm. On the other hand, the attraction ability is enabled when the first nanorobot adheres to the wound. It transmits attraction signal to others. The nanorobots that can sense the attraction signal know the approximate location of the wound and choose only the nanorobots transmitting signal as their neighbors; hence, the nanorobots could follow the signal and ultimately find the wound. The results suggested that the attraction signaling and sensing unit as well as blood velocity sensing unit could be included for characteristics of medical nanorobots in the future.

![Fig. 2 The comparison of the results from random movement, Canonical PSO (CanonicalPSO1), Canonical PSO with attraction signaling and sensing unit (CanonicalPSO2) and Canonical PSO with blood velocity sensing unit (CanonicalPSO3) for seeking the wound; (a) each line represents the median of the number of iterations over 10 runs against the perception range; (b) each line represents the median of the number of iterations over 10 runs against the number of time steps per second; (c) each line represents the median of time over 10 runs against the maximum velocity.](image-url)
VII. CONCLUSION

In conclusion, the canonical PSO can be used to control a swarm system of nanorobots with the essential characteristics, which are moving around the environment, carrying defined characteristics for the assembly task, connecting to another nanorobot at a specific area, operating inside human body with biocompatibility, and interacting with other nanorobots and its environment to operate as artificial platelets in circulatory system for seeking the wound. From the experimental results in the simulation of circulatory system, the performance of nanorobots with identified essential characteristics using canonical PSO based control mechanism is similar to the random movement approach. Nevertheless, introducing the ability to sense the external changes in the environment and the attraction ability between nanorobots at the optimal locations and other nanorobots in the area could enhance the nanorobot performance for physical applications i.e. medical nanorobots. This study can be beneficial as guidelines for the development of nanorobots in medical applications. Our future work is to apply canonical PSO to control the nanorobots to self-assemble into a plug at the wound site in order to assist the hemostasis process.

ACKNOWLEDGMENT

This study is supported by National Research Council of Thailand (NRCT).

REFERENCES