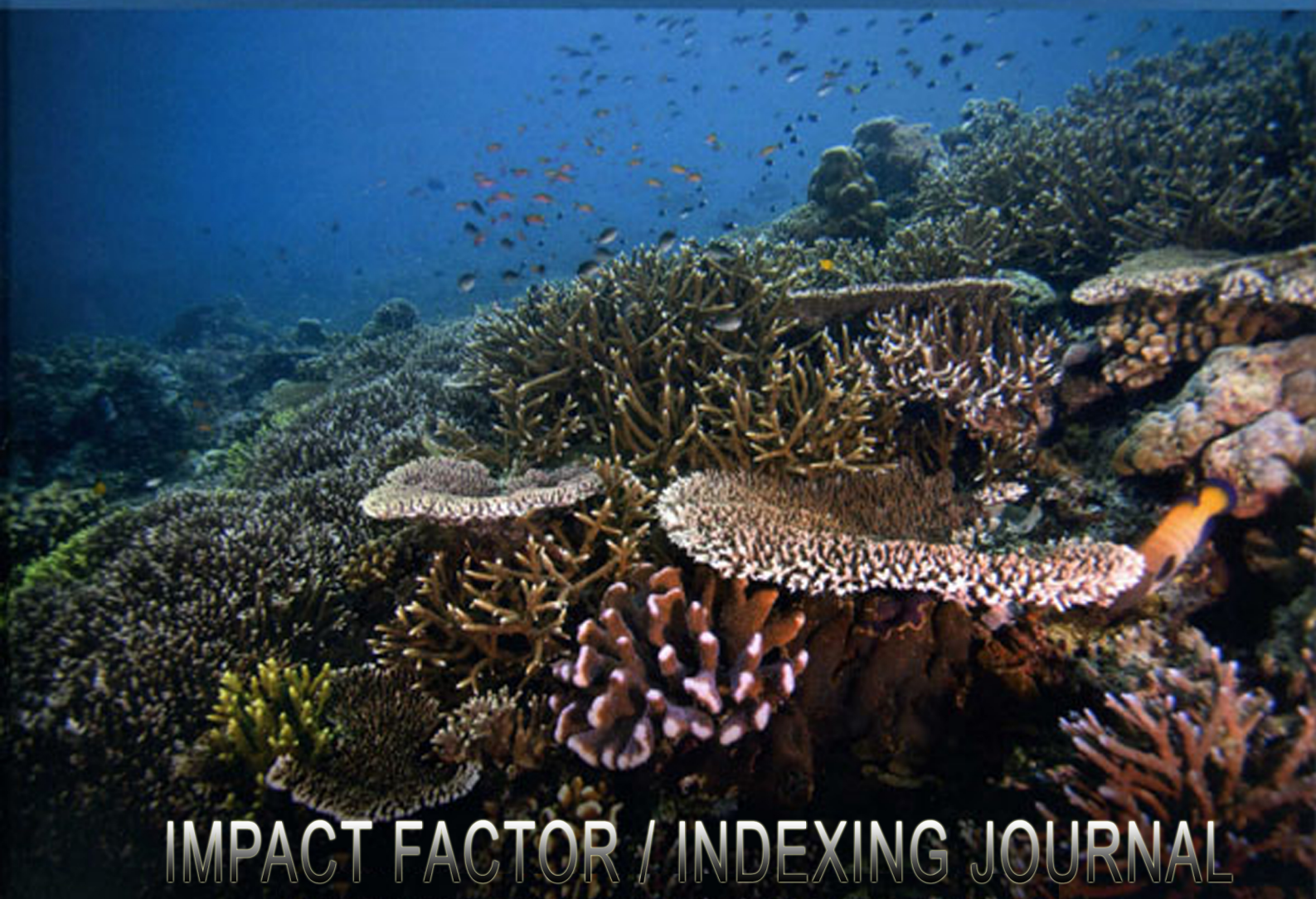


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SWARM INTELLIGENCE ALGORITHM FOR CANCER TREATING NANOROBOTS: A REVIEW

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ABSTRACT

Nanorobots are future in-vivo surgeons that will locomote in human vascular system manoeuvring their specific medical task such as identifying and destroying cancer cells, repairing tissues, clinical trials and so on. Since, they are expected to carry out complex tasks with their simple designs; they need a swarm intelligence system, that will ensure their collaboration, biocompatibility of these nanorobots as well as ability to adapt in dynamic environment in human body. Many Swarm Algorithms have been suggested so far for nanorobot functioning in vivo. In this Review, three major swarm algorithms are discussed, namely: Ant Colony Optimization (ACO), Particle Swarm Optimization (PSO) and Artificial Bee Colony Optimization (ABC). Many other algorithms are derived from these three algorithms. Their application in vivo for Cancer treatment is detailed and major problems based on their design and function, with respect to their collaborated biocompatibility are analysed. Possible solutions are suggested to overcome these problems so that Nanorobots may find their actual application in the field of medicine.

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INTRODUCTION

Cancer research is one of the leading research areas in the field of biotechnology since few decades. Cancer is one of the major causes of deaths worldwide (Gianni Di Caro *et al.*, 2005) and it can be seen that number of people suffering from Cancer is growing at an alarming rate per year. The existing treatment of Cancer such as Radiotherapy, Chemotherapy etc, are widely used without any effective counter for their harmful side effects. These techniques are non-specific and account for toxic after effects. Recently, researchers have converged emerging technologies to provide targeted therapies for cancer treatment with minimum side effects, (Arosha Senanayake *et al.*, 2007) Nanotechnology, with its ability to deal at atomic and molecular level, (Sanchita Paul *et al.*, 2012, Sharma *et al.*, 2008, Ummat *et al.*, 2007), can provide more than one solutions to the problem at hand. Use of Gold nanoparticles is extensively developed in target specific killing (Robert *et al.*, 2005, Sabine Hauert *et al.*, 2013) of cancerous cells. Further, the Researchers are studying the feasibility of nanorobots, which are assembly of nano components into a functional single entity, (Robert *et al.*, 2005, Sabine Hauert *et al.*, 2013, Arosha Senanayake *et al.*, 2007), which is capable of stimulating in human vascular

system, identifying target site, (Khin Haymar Saw Hla *et al.*, 2008, Masudur Rahman *et al.*, 2011, Arosha Senanayake *et al.*, 2007, Adriano Cavalcanti *et al.*, 2007) and destroying cancerous cells on its own without much external stimulus. In other words, these are pre-programmed engineered devices (Khin Haymar Saw Hla *et al.*, 2008), that can be employed to compute senses, signalling, and processing information and actuate at microscopic level, (Khin Haymar Saw Hla *et al.*, 2008, Tag Hogg *et al.*, 2006, Arosha Senanayake *et al.*, 2007) with precision.

Possibility of these tiny in vivo surgeons was seen as early as in 1950's when American Physicist quoted "There is plenty of room at the bottom", (Heusala *et al.*, 2007, Ummat *et al.*, 2007). It suggests the vastness of potential medical applications based on the effectiveness, precision, speed, reduced cost, risk, invasiveness and complexity of these tiny surgeons. Apart from Cancer treatment, these can be employed in clinical trials (Adriano Cavalcanti *et al.*, 2007), clearing artery blockages, (Ghada *et al.*, 2012, Adriano Cavalcanti *et al.*, 2007) repairing tissues, (Adriano Cavalcanti *et al.*, 2007) monitoring chemicals and their concentration in blood, (Khin Haymar Saw Hla *et al.*, 2008, Adriano Cavalcanti *et al.*, 2008, Adriano Cavalcanti *et al.*, 2007), biomedical instrumentation surgery (Mohammadjavad Abbasi *et al.*, 2011, Sanchita Paul *et al.*, 2012, Tag Hogg *et al.*, 2006, Masudur Rahman *et al.*, 2011) and so on. For their effective utility, they need to be

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Type-D power Grid Township, Dehradun road, Near puhana, Roorkee, 247667, Uttarakhand, India

employed in large numbers, (Heusala *et al.*, 2007). Since due to dimension limitations, much complex architecture of a nanorobot is not feasible, they need to exhibit complex behaviour with their simple design, (Sabine Hauert *et al.*, 2013). Hence, an effective swarm Intelligence is needed to be employed. Swarm intelligence is a system where numerous simple components interact with one another as well as environment, (Simon Garnier *et al.*, 2007, Hazem Ahmed, *et al.*, 2012), to produce a big-complex result, (Sabine Hauert *et al.*, 2013, Yang Liu and Kevin *et al.*, 2015). Number of nanorobots will be injected into the blood vessel (Masudur Rahman *et al.*, 2011), thus in order to avoid random actions of all the individual units, it is essential to establish co-ordination so that they can interact with one another and synchronize their tasks in space and time (Simon Garnier *et al.*, 2007, Ummat *et al.*, 2007, Sabine Hauert *et al.*, 2013) For effective co-ordination, well means of communication and task allocation is essential, (Simon Garnier *et al.*, 2007). A proper swarm intelligence system will enable these tasks without much design complexities or biohazard. While artificial devices such as nanorobots are functioning in body without much external stimulus, it is major responsibility of the established swarm system to bring about adaptability to the changing environmental conditions *in vivo* (Ghada *et al.*, 2012), ensure that no nanorobot is lost in the body during exploration (Ghada *et al.*, 2012), target site is correctly identified and traffic routes are established in blood vessels in order to avoid any blockages.

Background and Motivation

Concept of nanorobots has been inspired from micro-organisms, (Tag Hogg *et al.*, 2006, Sharma *et al.*, 2008, Heusala *et al.*, 2007). Theoretical designing of nanorobots has been going on since a couple of decades by integrating the fields of Nano-biotechnology (Masudur Rahman Al-Arif *et al.*, 2011, Ummat *et al.*, 2007), which offers wide variety of biological molecules with sensory and motor actions and artificial intelligence (Khin Haymar Saw Hla *et al.*, 2008, Tag Hogg *et al.*, 2006, Ummat *et al.*, 2007), and Nano-electronics based embedded systems: CMOS technology (Complementary Metal Oxide Semiconductor), (Khin Haymar Saw Hla *et al.*, 2008, Sanchita Paul *et al.*, 2012, Sharma *et al.*, 2008, Masudur Rahman Al-Arif *et al.*, 2011, Heusala *et al.*, 2007, Adriano Cavalcanti *et al.*, 2007, Adriano Cavalcanti *et al.*, 2008). Manufacturing nanorobots constitutes of series of steps which starts with determining feasibility of the concept theoretically. It is followed by detailed computational simulations of nanorobot components, their assemblies and then full system simulations using Nanorobot Control Design (NCD) simulators, (Tag Hogg *et al.*, 2006).

Once simulations are done, factories perform manufacturing simulations and later fabrication, assembly testing and clinical trials, (Mary Mehrnoosh *et al.*, 2009, Mary Mehrnoosh *et al.*, 2008, Adriano Cavalcanti *et al.*, 2008). Robert A. Freitas Jr, who is a senior researcher in IMM, Palao Alto California did major research work in medical nanorobotics, molecular machine design, molecular assemblers and self-replication in machine and factory system, (Robert *et al.*, 2005). He is author of 4- volume series of books Nanomedicine (Sanchita Paul *et al.*, 2012), first volume of which was published in 1999. Since then, researchers all around the globe have carried out

researches on various medical applications of nanorobots and their designing. Nanorobots are positional assembly of the units such as nanotubes (Sharma *et al.*, 2008, Robert *et al.*, 2005), nanofibres, nanoshells (Sharma *et al.*, 2008, Robert *et al.*, 2005), actuators, nano electronic circuits based on CMOs transducers, (Adriano Cavalcanti *et al.*, 2008, Adriano Cavalcanti *et al.*, 2007, Adriano Cavalcanti *et al.*, 2008), nanowires, (Khin Haymar Saw Hla *et al.*, 2008, Robert *et al.*, 2005, Adriano Cavalcanti, Bijan Shirinzadeh *et al.*, 2008), photonics (Robert *et al.*, 2005, Mustapha Hamdi *et al.*, 2008), biosensors (Ghada Al-Hudhud *et al.*, 2012, Khin Haymar Saw Hla *et al.*, 2008, Sanchita Paul *et al.*, 2012, Adriano Cavalcanti *et al.*, 2008), artificial binding sites (Robert *et al.*, 2005), etc. A variety of biological as well as synthetic nano computers have been devised which are essential component onboard since it provides nanorobot complete internal control to conditionally execute tasks in dynamic *in vivo* environment (Sanchita Paul *et al.*, 2012). An actuator (Masudur Rahman Al-Arif *et al.*, 2011), with biologically-based components has also been proposed. This actuator has a mobile member that moves substantially linearly as a result of a bio-molecular interaction between biologically-based components within the actuator, (Ummat *et al.*, 2007, Adriano Cavalcanti *et al.*, 2008).

Such actuators can be utilized in nanoscale mechanical devices to pump fluids, open and close valves, or to provide translational movement, (Khin Haymar Saw Hla *et al.*, 2008). Cancer treating nanorobots have nano-biosensors on the surface that detect various levels of E-Cadherin as medical targets and help in target identification and drug delivery (Ghada Al-Hudhud *et al.*, 2012, Khin Haymar Saw Hla *et al.*, 2012, Mohammadjavad Abbasi *et al.*, 2011, Chandrasekaran, *et al.*, 2006, Tag Hogg *et al.*, 2006, Masudur Rahman Al-Arif *et al.*, 2011, Adriano Cavalcanti *et al.*, 2008). Many swarm intelligence algorithms based on the concept of insects (Dervis Karaboga *et al.*, 2009, Hazem Ahmed *et al.*, 2012, Gianni Di Caro *et al.*, 2005), have been suggested for the problem at hand. Insects are compared to nanorobots as elaborated "machines", with the ability to modulate their behaviour on the basis of processing of many sensory inputs, to cope with uncertain situations or solve problem at hand collectively. In his novel "Prey", Crichton describes a swarm of artificial insect-like nanorobots which is governed by such a collective mind (Simon Garnier *et al.*, 2007), allowing them to take complex decisions and even to anticipate future events.

In designing an efficient swarm algorithm, incorporation of certain concepts such as stigmergy, (Simon Garnier *et al.*, 2007, Hazem Ahmed *et al.*, 2012), decentralization (Tag Hogg *et al.*, 2006, Hazem Ahmed *et al.*, 2012, Ummat *et al.*, 2007), self-organization (Khin Haymar Saw Hla *et al.*, 2008, Simon Garnier *et al.*, 2008, Ummat *et al.*, 2007), bifurcations, (Simon Garnier *et al.*, 2008) and positive-negative feedbacks, (Simon Garnier *et al.*, 2008) are essential. Stigmergy lays emphasis on guidance of local environment to regulate activities of individual unit in a swarm. Complete centralization is not possible (Khin Haymar Saw Hla *et al.*, 2008), for the system *in vivo* since, no individual nanorobot can access swarm globally, monitor and direct actions of the subordinate nanorobots (Ghada Al-Hudhud *et al.*, 2012). In such a case, supervisor nanorobot will require highly complex architecture and organization. Thus, concept of decentralization is easily

employed in swarms in which, actions of units are directed by local stimulus without knowledge of global pattern (Ghada Al-Hudhud *et al.*, 2012, Khin Haymar Saw Hla *et al.*, 2008, Tag Hogg *et al.*, 2006). Secretion of certain chemical concentrations can determine positive and negative feedbacks in a swarm. These feedbacks, their amplifications along with stigmergy create self-organization in a swarm. Self-organization is a set of dynamical mechanisms whereby structures appear at the global level of a system from interactions among its lower-level components, without being explicitly coded at the individual level, (Khin Haymar Saw Hla *et al.*, 2008, Simon Garnier *et al.*, 2007).

Swarm Behaviour

Major means of communication between two nanorobots in a swarm is found to be via chemical molecules, (Ghada Al-Hudhud *et al.*, 2012). Each nanorobot will secrete a certain chemical molecule with the purpose of signalling, while they will also have chemotactic sensors, (Tag Hogg *et al.*, 2006) onboard to sense such chemical signals and their concentrations. Such type of system is called Quorum sensing, (Nantapat *et al.*, 2011, Chandrasekaran *et al.*, 2006, Tag Hogg *et al.*, 2006, Heusala *et al.*, 2007). Quorum sensing enables nanorobots to communicate as well as coordinate their tasks. From the concept of quorum sensing, theory of Attractants emerged. Attractants, (Chandrasekaran *et al.*, 2006) are said to be specific chemical molecules for which each nanorobot in a system has affinity. These are secreted by those nanorobots that have already identified the target site, to accelerate the movement of rest of the swarm towards the target site. Of all the advantages of the Attractant theory, one of the major advantage is that it enables oncoming nanorobots to determine whether sufficient nanorobots are present at the site of action/target site or not, on the basis of the concentrations of attractants, (Ghada Al-Hudhud *et al.*, 2012, Tag Hogg *et al.*, 2006). However, if applied to real time applications, Attractant molecules may cause collisions among nanorobots due to their affinitive nature, leading to either their fragmentation and loss of control or jamming into nearby soft tissues. Sensing and motion are the two most important actions of a nanorobot in target identification. Hence they are defined into three types:

Multi-directional Sensing and Motion

In such a system, each nanorobot has 2 motors and more than 2 sensors present on different directions. It constantly senses the chemical signals present in its environment in multiple directions and compares them. Then it moves towards the signal with higher concentration.

Mimic Bacterial sensing and Motion

Each nanorobot has only one sensor and one motor. It spans its environment for any chemical signal gradient after a specific time interval which is pre-defined and pre-programmed. It moves randomly with a blood flow unless it encounters sum concentrations of chemical signals.

Random Motion

Each nanorobot with one sensor and one motor, flows randomly with the blood without searching for concentration

gradients. It often finds its target site by random contact during its flow movement, (Nantapat *et al.*, 2011, Chandrasekaran *et al.*, 2006). Selection of any of the above system should depend primarily on its major application and goal. For example, for nanorobots that measure concentration of certain chemicals in blood plasma, such as insulin in case of diabetes, random motion can be easily applied. In such a system, not much of the energy is consumed, since nanorobot mostly flow with the blood and does not have to find a specific target site. While in case of Nanorobots whose major goal is to find and treat a target specific disease such as Cancer or artery blockage, Multi-direction sensing and motion is most suggestible for complete exploration. For a nanorobot, to reach target site, two methods are described majorly. As mentioned previously: Random Motion and Follow Gradient Khin Haymar Saw Hla *et al.*, 2008, Sanchita Paul *et al.*, 2012, Tag Hogg *et al.*, 2006).

Numerous algorithms have been suggested and applied to computer simulations of medical nanorobots. However, for cancer treating nanorobots, majorly three algorithms have been discussed, namely: Ant Colony Optimization (ACO), Particle Swarm Optimization (PSO) and Artificial Bee Colony Optimization (ABC). Many other algorithms are derived from these three algorithms (Shu-Chuan Chu *et al.*, 2011). These three major algorithms are discussed keeping certain assumptions into consideration: These nanorobots are non-self replicating devices (Arosha Senanayake *et al.*, 2007), small to facilitate movement in the smallest of capillary, biocompatible with human immune system (Ghada Al-Hudhud *et al.*, 2012, Sanchita Paul *et al.*, 2012, Tag Hogg *et al.*, 2006, Arosha Senanayake *et al.*, 2007) and other chemical and mechanical factors, (Sharma *et al.*, 2008, Robert *et al.*, 2002), have inbuilt power supply (Adriano Cavalcanti *et al.*, 2008), are able to withstand the Brownian motion (Sharma and Mittal, 2008) and viscous forces, (Tag Hogg *et al.*, 2006, Sharma *et al.*, 2008), are programmed to move as close to vessel wall as possible, (Tag Hogg *et al.*, 2006, Sharma *et al.*, 2008) and will stay temporarily in body until their specific purpose is completed.

Ant Colony Optimization (ACO)

It was first given by Dr. Marco Dorigo, in collaboration with Alberto Colomi and Vittorio Maniezzo in 1991, (Nada *et al.*, 2009, Vittorio Maniezzo *et al.*, 2001, Hazem Ahmed *et al.*, 2012). It is based on the behaviour of ants (Vittorio Maniezzo *et al.*, 2001, Gianni Di Caro *et al.*, 2005), in a colony. The fundamental approach behind ACO is an iterative process in which a population of simple agents repeatedly construct candidate solutions; this construction process is probabilistically guided by heuristic information (Vittorio Maniezzo *et al.*, 2001), on the given problem instance as well as by a shared memory containing experience gathered by the ants in previous iteration, (Nada *et al.*, 2009). It is noted that ants initially move randomly in all different directions in search of food. Each ant leaves a pheromone (Hazem Ahmed *et al.*, 2012), trail behind that has tendency to evaporate after some time. This pheromone acts as an attractant to the other ants of the colony and they follow the trail that has been left behind by the previous ants. Pheromone trail tends to evaporate on longer trails while on shorter trail, it is more prominent, and hence, shorter trail is further followed by other ants (Nada *et al.*, 2009, Simon Garnier *et al.*, 2007), one after another, leading to the increase in the attractiveness of the

trail. Thus, approach can be applied to find target site by shortest route. Pheromone levels are modified at run-time and leads to the updating of route information by trail evaporation, (Vittorio Maniezzo *et al.*, 2001) and pheromone updates (Nada *et al.*, 2009). Results of the approach depend upon trail and their respective attractiveness, (Nada *et al.*, 2009, Vittorio Maniezzo *et al.*, 2001). Principles of self organization are used to coordinate population of artificial units, (Nada *et al.*, 2009). Prior information about the structure of promising solution is combined with posterior information about the structure of previously obtained good results, (Vittorio Maniezzo *et al.*, 2001). Main steps (Nada *et al.*, 2009), in this algorithm are:

- 1: Set initial parameters of the system
- 2: Set initial pheromone trail values
- 3: While (results are not met)
 - Construct Ant solutions
 - Apply local search
 - Best tour check
 - Update trail
- 4: End while

Apart from computational problem, this approach was also assessed for medical nanorobots with goal of finding cancer site in body and treating it. Consider a swarm of nanorobots, all designed alike, is injected into the human vascular system. Many nanorobots of the swarm will move randomly with the blood flow leaving pheromone trail behind. These pheromone trails will attract other nanorobots of the swarm. Pheromone trail of those nanorobots, which drift off far with the blood without having detected any chemical concentration gradient from the target site, will eventually be lost. While trails of those nanorobots, which are followed by a large swarm and having found concentration gradient from target site comparatively quickly, will be updated more often by pheromone. Hence, becoming only traffic route to target site from the site of injection.

However, ACO cannot find its practical application in cancer treatment since problem space for nanorobots *in vivo* is much dynamic due to Brownian motion of blood plasma (Tag Hogg *et al.*, 2008). Due to such environment, pheromone trails can get disturbed and hence, unpredictable. Trails can never be laid against the blood flow. Since trail is major basis for functioning of swarm system, it can lead to collapse of entire system and loss of adaptability, (Nada *et al.*, 2009). Further, ACO is more a probabilistic approach (Nada *et al.*, 2009), it does not guarantee complete exploration of all the target sites. Once the shortest route to a nearby target site is found, swarm may not explore and cure the other areas that might be infected with cancer. In such a system, there is greater probability of collision of nanorobots among themselves, (Robert *et al.*, 2002) and no account for retrieving those nanorobots that are separated from swarm and lost during exploration.

Particle Swarm Optimization (PSO)

It was first given by Dr. Eberhart and Dr. Kennedy in 1995, (Dervis Karaboga *et al.*, 2009, Mohammadjavad Abbasi *et al.*, 2001, Simon Garnier *et al.*, 2007, Simon Garnier *et al.*, 2012, Shu-Chuan Chu *et al.*, 2011). It is inspired from the behaviour of flocking birds and schooling fishing (Dervis Karaboga *et al.*, 2009, Micael *et al.*, 2011). PSO gives a complete control

on the mobility of nanorobots *in vivo*. In this approach, each particle is programmed to move in a pre-defined path in a problem space, keeping track of its own coordinates called p-best or particle best (Dervis Karaboga *et al.*, 2009), position, which are associated with best results. It constantly scans the positions of nearby particles and their trajectories. As soon as it finds any position better than its current position called l-best or local best (Dervis Karaboga *et al.*, 2009), position, it moves to it with modified velocity. The position which is best with respect to the entire swarm is called g-best position (Micael *et al.*, 2011, Khin Haymar Saw Hla *et al.*, 2008, Mohammadjavad Abbasi *et al.*, 2011, Shu-Chuan Chu *et al.*, 2011). Main steps (Dervis Karaboga *et al.*, 2009), in this algorithm are:

- 1: Initialize population
- 2: While (results are not met)
 - Calculate fitness values of particles
 - Modify the best particle in the system
 - Choose the best particle
 - Calculate the velocities of the particle
 - Update the particle positions
- 3: End while

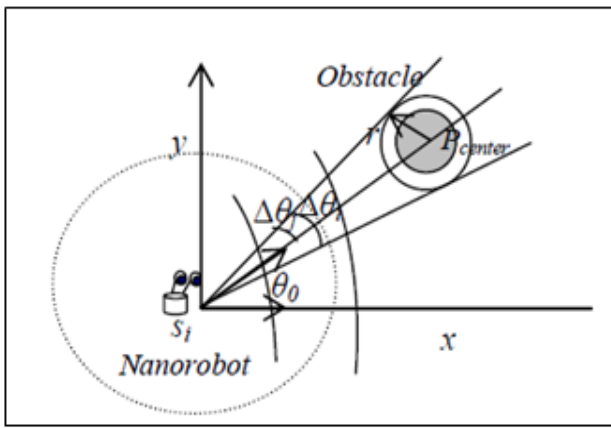
PSO can be better understood by understanding the three rules given by Reynolds that synchronize the movement of flocks: Cohesion, Separation and Alignment.

Cohesion Rule: The cohesion rule (Ghada Al-Hudhud *et al.*, 2012, Hazem Ahmed *et al.*, 2012), acts as a binding force. It reinforces each swarm member to orient its velocity vector towards the centroid of the team members that fall in the field of view of this rule. For each swarm member, located at corresponding positions, the centroid of this rule is computed as the distance to the average of the positions of the detected located at position. The swarm member computes the distance to the centroid and a correction angle. As a result this rule always implies the member move toward the centroids of the flock, cohere with the team. Thus tendency of any particle to get separated from the swarm is minimized, (Ghada Al-Hudhud *et al.*, 2012).

Separation Rule: Also known as collision avoidance rule Ghada Al-Hudhud *et al.*, 2012, Hazem Ahmed *et al.*, 2012], it serves for the purpose of keeping a minimum required distance of the particle from the nearby obstacles. It is done so by sensing the obstacles in the path of the particle and calculating their trajectory and planning self trajectory accordingly. For application in nanorobots, it can be done by determining the structure of obstacle in polar coordinate system and then find the best possible trajectory for avoiding the collision, (Khin Haymar Saw Hla *et al.*, 2008, Sanchita Paul *et al.*, 2012).

$$\text{Obstacle} = \langle P_{\text{centre}}, P_{\text{radius}}, P_{\text{velocity}} \rangle$$

Above mentioned are polar coordinates of a moving obstacle in the problem space. Using the information about the angle of projection of the obstacle, nanorobot can effectively compute a desirable direction angle for its own movement trajectory (Khin Haymar Saw Hla *et al.*, 2008). Also a nanorobot constantly calculates the minimum separation distance from its swarm members in order to avoid hitting each other, (Ghada Al-Hudhud *et al.*, 2012)



Alignment Rule: This rule is also known as a velocity matching rule (Hazem Ahmed and Janice Glasgow, 2012 and Shu-Chuan Chu *et al.*, 2011) as each swarm member tries to detect nearest member from the same team and getting the velocity of this member. Hence, calculates the correction angle to align with the nearest member. The sensory data is filtered for this rule to pick only the nearest friend, a detected neighbour from the same team. The sensor range and the field of view define the perception zone for this rule. The alignment rule results in a velocity vector an agent should follow to modify its current direction in order to align with this neighbour, if found. For member, the velocity vector composes a centroid and a correction angle. The centroid of this rule is considered as the distance to position at. The correction angle is computed as the difference between the current heading and the heading angle of the nearest member (Ghada Al-Hudhud *et al.*, 2012, Shu-Chuan Chu *et al.*, 2011).

These three rules apply to the system at Local Communication level (Ghada Al-Hudhud *et al.*, 2012) where all the particles of the swarm are interacting with one another, sending messages via electrical and chemical signals (Khin Haymar Saw Hla *et al.*, 2008). Actions of all the particles are decentralized, depending upon the environmental stimulus. Another alternative is Global Communication, (Ghada Al-Hudhud *et al.*, 2012) level where all the Task assignment and communication is centralized via external source (medical physician in case of cancer treating nanorobots). PSO was originally used to solve non-linear continuous optimization problems (Dervis Karaboga *et al.*, 2009), but more recently it has been used in many practical, real-life application problems such as to track dynamic systems, evolve weights and structure of neural networks etc. However, their application to a system of cancer treating nanorobots is less practical than it originally appears since; it requires a pre-operative path planning which possible if the problem space is small but not in larger and dynamic environment (Micael *et al.*, 2011) such a human vascular system.

For applying above mentioned three rules, a nanorobot requires means of lot of computation, (Mohammadjavad Abbasi *et al.*, 2011) as well as energy. Further, due to Cohesion rule, if any one of the nanorobot is trapped at a place, the entire swarm associated with it will be trapped into their local minimum, (Micael S. Couceiro *et al.*, 2011). Hence, PSO's application in Cancer Treatment does not guarantee optimal solution. It fails to matches one of the major need for the requirement of the swarm system, which is reducing design complexity of each nanorobot.

Artificial Bee Colony Optimization (ABC)

Artificial Bee Colony Optimization was first suggested by Karaboga in 2005 (Dervis Karaboga *et al.*, 2009, Dervis Karaboga and Celal Ozturk *et al.* 2010, Hazem Ahmed *et al.*, 2012, Shu-Chuan Chu *et al.*, 2011), based on behaviour of Bees. It is an algorithm based on collaboration and coordination (Dervis Karaboga *et al.*, 2009) Bees achieve their task of finding food by dividing their roles. This feature of task division makes it quite distinct algorithm from previous ones. Here Bees are divided into three types: Employed bees, Onlooker bees and Scout bees, (Ghada Al-Hudhud *et al.*, 2012, Dervis Karaboga 2009). These three types of bees tend to perform different functions. Employed bees stay on the discovered food source and continuously send coordinated of the target to the onlooker bees that stay at the hive unless they receive coordinates of food by Employed bees. Meanwhile scout bees are the employed bees whose food source has been abandoned by onlooker bees, and they search for different food source in the target space (Dervis Karaboga *et al.*, 2009, Dervis Karaboga and Celal Ozturk *et al.*, 2010, Simon Garnier *et al.*, 2007, Nantapat *et al.*, 2011) This algorithm is also a decentralized system where the working and result greatly depend on the environmental stimulations. The system of task allocation can reduce the design complexities in each nanorobot, as each nanorobot will be equipped with those nano-instruments which are required only for its specific function. Features of swarm such as stigmergy, bifurcations, self organization and positive- negative feedbacks are completely utilized in such a system. Whole approach is entirely based just to find the optimal or best solution of the problem. Main steps (Dervis Karaboga *et al.*, 2009) in this algorithm are:

- 1: Initialize population
- 2: While (results are not met)
 - Place the employed bees on the food sources
 - Place the onlooker bees on the food sources depending on their nectar amounts
 - Send the scouts to the search area to search new food sources
 - Memorize the best food source so far
- 3: End while

This approach was basically designed to apply on medical nanorobots (Dervis Karaboga *et al.*, 2010), whose main aim is to find a target site, such as Cancerous site. Consider, a swarm of medical nanorobots is injected into the human vascular system closest to the target site possible. Swarm consists of three types of nanorobots who are differently designed. Soon after the injection, while rest of the swarm stays at the site of injection, some of the nanorobots (employed) start moving randomly along with the blood flow in search of the target site. As soon as they find some concentrations of E-Cadherin, they follow Concentration Gradient to reach the target site. On reaching the target site, they adhere themselves to the cancer cells and start sending out acoustic signals (e.g. RF signals) which when received by other swarm (onlooker) which is present at injection site, activates them and they move towards the source of signals like the concept of attractant. Now, this system may or may not prove to be successful when applied in real life problems, but it is definite that this system needs some modifications to turn it into a foolproof approach. When we

study its application, many questions arise: While onlooker swarm is working on a Cancer site, they receive signal from a different employed nanorobot, will they leave the task at hand unfinished to move to another site? What if any employed nanorobot is lost while exploring the problem space for a target site due to the dynamic environment? Is there any possibility of blood vessels getting blocked by swarm (onlooker) movement? There is no focus laid on the traffic routing of the swarm while moving, so that they do not block the blood vessels or their concentration in blood plasma does not reach greater than 10% for unaltered viscosity of blood with respect to the vessel walls (Sharma *et al.*, 2008). Further there is no system to ensure that all the nanorobots in the swarm stay together, or the ones which are lost can be retrieved. All though it guarantees complete exploration (Dervis Karaboga *et al.*, 2010), it does not give optimized results unless modified. By few modifications in the system, greater degree of adaptability can be achieved.

Chemical Based ABC Swarm Intelligence Algorithm: With a little modification in ABC, the above problems in the Swarm system *in vivo* can be solved. In the task allocating system ABC, pheromone trail concept of ACO has been combined to create definite traffic routes. This traffic routing ensures that blood vessels are not blocked during the swarm movement and at no point of time their concentration in blood plasma crosses a certain value that can affect the viscosity of blood with respect to the vessel walls. Further, this guarantees the return of any lost nanorobot to the swarm because of its affinity for the pheromone trail on its own accord. Nanorobots obtain their sense of direction by two switching onboard chemo-tactic sensors (Tag Hogg *et al.*, 2006), one for E-Cadherin and other for pheromone molecules. Nanorobots can be divided into two types: Lookout and Worker Nanorobots. Both differ in their designs according to the need. While Worker Nanorobots (WN) have both target specific and attractant or pheromone specific sensors active simultaneously, in Lookout Nanorobots (LN) functionality of these two sensors switch if their specific threshold values are met. Pheromone or attractant molecule define traffic routes to the target site, (Sharma *et al.*, 2014). It can be a time consuming approach, but can guarantee complete exploration and optimal results. Major steps in this algorithm are:

- 1: Initialize population
- 2: While (results are not met)
 - Target specific sensor of Lookout nanorobots activated
 - Threshold values of target molecules, switching of sensor
 - Attractant specific sensor activated, to find swarm
 - Threshold values of attractant, switching of sensor
 - RF signal activates inactive Worker Nanorobots
 - Threshold value of target molecules, Worker Nanorobot deliver drug
- 3: End while.

Future

Medical nanorobots are still in their simulation stage. Some minor designs of nanorobots have been produced but a foolproof self sufficient *in vivo* surgeon is yet to be designed. Size limitations pose a major problem in the designing. Currently, nanorobots whose propulsions will be based on imaging techniques are being worked upon. Swarm system is one of the factors that again pose a problem for their *in vivo*

applications. The day when a biocompatible swarm system is designed, there will be a great revolution in the field of medicine. Word biocompatible not only refers to biological factors, but also physical, chemical and mechanical factors that affect the functioning of nanorobots *in vivo*. Much work is still needed to be done in developing a nanocomputer with efficient memory retention, so that a completely independent and automatic nanorobot can be employed *in vivo*.

Conclusion

Nanomedicine stores potential to wipe out all the common and uncommon hailing ailments in present as well as to-come century. New therapeutic applications of nanoparticles are already being discovered every day, and with the introduction of nanorobots, we might not need manual surgeons any more in days to come. But to make this technology such reliable, we not just need to develop perfect subsystems for nanorobots, but also a better Swarm system. A swarm system should be designed for a nanorobot swarm considering the task to be performed by them in such a manner that method of getting the work done and designs of nanorobot are biocompatible. Meanwhile, it aims to achieve efficient results and prevent maximum biohazard

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