

APPLICATION OF EULAR METHOD TO COMPLETE DIFFERENTIAL EQUATION IN MAGNETIC MEDICINE SIMULATION

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ABSTRACT

Along with technological developments, the study of magnetic nanoparticles was a concern to scientists and engineers. One of the most widely synthesized types of nanoparticles was the nanoparticles used in medicine because it had magnetic properties, which were properties that could be drawn by the magnetic field and it was this character that useful for human life in various fields.

The research for solves differential equations by using Euler method with Matlab simulation program to simulate the movement of drugs human body. From the simulation, we have the results of the data that shows the velocity of drug particles depends on time due to the influence of a strong magnetic field. The duration takes for the particles to find the magnetic field is 40 seconds. We divide final position of the particle distribution with 20 classes. Distribution of particles in the interval -0,3 to -0,1 have the smallest percentage of the particle distribution is 0,3% and the particles in the interval of 0,6 to 0,8 have the largest percentage is 2,2%. By using the exponential function approach to predict the average velocity it is concluded that the function $f(t) = A \exp(-kt)$, with the value of function $A = 1$ and $k = 0,8$ the closest.

KEYWORDS: Magnetic Nanoparticles, Euler Methods, Magnetic Field, and Particle Distribution

1. INTRODUCTION

Nanomaterials are a rapidly growing field of nanotechnology (Babincova & Babinec, 2009). Research on magnetic nanoparticles (MNPs) has been increasing over the last decade due to widespread use in various fields (Gawali, Barick, Barick, & Hassan, 2017; O'Donnell, 2018). Various applications of magnetic nanoparticles are promising in the field of technology and biomedicine, particularly for increased delivery of targeted drugs and magnetic hyperthermia. However, for the magnetic properties of nanoparticles, information on particle structure is paramount (Alemzadeh, Dehshahri, Izadpanah, & Ahmadi, 2018; Bautin, Seferyan, Nesmeyanov, & Usov, 2018). Ideally, the nano delivery system may allow for the targeting of more specific drugs, thereby enhancing efficiency and minimizing side effects. Design and delivery (distribution) of drugs (Yang et al., 2018), researchers are trying to develop nanomedicine to be able to deliver drugs to targeted tissues, release the drug at a controlled level, into a biodegradable drug delivery system. (Bharali Marianne Khalil Mujgan Gurbuz Tessa M Simone Shaker A Mousa, 2009). The magnetic parameters for nanoparticles are Fe_3O_4 (Babincova & Babinec, 2009; Bautin et al., 2018). The magnetite nanoparticles are formed according to the following reaction (Babincova & Babinec, 2009; Rayegan, Allafchian, Abdolhosseini Sarsari & Kameli, 2018)



1.1. Drug Targeting Magnetization

The forces acting on some magnetic particles in the fluid and magnetic environments, such as the Stokes viscosity tensile force, the moment of inertia, buoyancy, and gravity, thermal kinetics (Brownian motion). The interaction of magnetic tensile force and viscosity to magnetic nanoparticles forms a magnetic dipole interaction. On the motion of magnetic particle motion in the magnetic field and viscous fluid using Newton's law (Babincova & Babinec, 2009):

$$m_p \frac{dv_p}{dt} = F_m + F_s \quad (1.1)$$

Where m_p dan v_p is the mass and velocity of the particles, dan F_m dan F_s are the magnetic pull force and the Stoke force. The magnetic force acts on a particle, where the magnetic particles are replaced by the dipole point when m_p , e_{ff} is localized at the center of the particle. According to this method, the dipole is given by:

$$F_m = \mu(m_{p,eff} \cdot \nabla) H_a \quad (1.2)$$

Where μ s the permeability of the ambient fluid, $m_{p,eff}$ is the dipole moment when the particle, which depends on the external plane is applied H_a the magnetic intensity at the center of the particle, where the dipole moment is localized. Therefore, the magnetic saturation at the effective dipole moment can be

$$m_{p,eff} = V_p f(H_a) H_a \quad (1.3)$$

Taking into account magnetic particles with R_p radius dan volume V_p , and functions

$$f(H_a) = \begin{cases} \frac{3(\chi_p - \chi_f)}{(\chi_p - \chi_f)^3} H_a < \frac{(\chi_p - \chi_f)^3}{3\chi_p} M_{sp} \\ M_{sp}/H_a & H_a \geq \frac{(\chi_p - \chi_f)^3}{3\chi_p} M_{sp} \end{cases}, (|\chi_f| \ll 1) \quad (1.4)$$

Where χ_p dan χ_f s the vulnerability of magnetic particles and ambient fluids, M_{sp} is the saturation of particle magnetization, and $H_a = |H_a|$.

($\chi_f \approx 0$) is a non-magnetic fluid and a high vulnerability of magnetic particles, ie $\chi_p > 1$, sin the case of water or air as ambient fluid, and magnetite (Fe_3O_4) as particles hence;

$$f(B/\mu) = \begin{cases} 3 B/\mu < M_{sp}/3 \\ M_{sp} \mu/B & B/\mu \geq M_{sp}/3 \end{cases} \quad (1.5)$$

Where B is the external magnetic field flux density and is applicable: $B/\mu = H_a$. Magnetic flux density is modeled as a magneto static problem with the euler method. In this case, the field intensity (H) and flux density (B) must satisfy the equation with the constitutive relationship between B and H for each material.

$$\nabla \times H = J \quad (1.6)$$

$$\nabla \cdot B = 0 \quad (1.7)$$

$$B = \mu H \quad (1.8)$$

The flux density is written in terms of potential in the vector \vec{A} , such as:

$$\mathbf{B} = \nabla \times \mathbf{A}, \quad (1.9)$$

In addition to the fluid magnetic force acting on a particle moving in a liquid medium. The magnitude is determined by Stokes' law on spheres with radius of R_p in a uniform flow, where η and v_f are the viscosity and velocity of the fluid, and v_p is the particle velocity. In this case the ambient fluid is ambient, i.e. $v_f = 0 \text{ m.s}^{-1}$ (Hoshiar, Le, Amin, Kim, & Yoon, 2017)

$$\mathbf{F}_s = -6\pi\eta R_p (\mathbf{v}_p - \mathbf{v}_f) \quad (1.10)$$

Magnetic flux densities were calculated using the Euler method analysis and used for particle path calculations. Movement of magnetic particles in a magnetic field with flux density B in the ambient fluid with a fixed η , viscosity represented by a system of ordinary differential equations:

$$\begin{aligned} \frac{dx}{dt} &= v_{p,x} \\ \frac{dy}{dt} &= v_{p,y} \\ \frac{dv_{p,x}}{dt} &= \frac{1}{m_p} \left\{ \frac{V_p}{\mu} f(B/\mu(x, y)) \left[+B_x(x, y) \frac{\partial B_x(x, y)}{\partial x} + B_y(x, y) \frac{\partial B_x(x, y)}{\partial y} \right] - 6\pi\eta R_p v_{p,x} \right\}, \\ \frac{dv_{p,y}}{dt} &= \frac{1}{m_p} \left\{ \frac{V_p}{\mu} f(B/\mu(x, y)) \left[+B_x(x, y) \frac{\partial B_y(x, y)}{\partial x} + B_y(x, y) \frac{\partial B_y(x, y)}{\partial y} \right] - 6\pi\eta R_p v_{p,y} \right\}, \end{aligned} \quad (1.11)$$

Where $m_p = V_p \rho_p$ dan $V_p = 4/3\pi R_p^3$ are the mass and volume of the particles. This system is derived from a combination of equations (1.1), (1.3), (1.5) dan (1.10) (Babincova & Babinec, 2009)

1.2. Euler Method

The Euler method is one of a simple one-step method of solving differential equations. Through a numerical approach it will obtain a continuous functional solution in the form of mesh points within the interval $[a, b]$. Having obtained a numerical solution at a point, then the other points can be searched by way of interpolation

A differential equation can be expressed as follows:

$$\frac{dy}{dt} = f(t, y) \quad (1.12)$$

The initial stage of the numerical approach solution is to determine the points within the same distance within the interval $[a, b]$, i.e. by applying

$$t_i = a + ih, i = 0, 1, 2, 3 \dots N \quad (1.13)$$

Distance between points is defined as

$$h = \frac{b-a}{N} \quad (1.14)$$

Euler's method is derived from the Taylor series. For example, the function $y(t)$ is a continuous function and has a derivative in the interval $[a, b]$. Then in the Taylor series

$$y(t_{i+1}) = y(t_i) + (t_{i+1} - t_i)y'(t_i) + \frac{(t_{i+1} - t_i)^2}{2} y''(\xi_i) \quad (1.15)$$

Because $h = (t_{i+1} - t_i)$, then

$$y(t_{i+1}) = y(t_i) + hy'(t_i) + \frac{h^2}{2}y''(\xi_i) \quad (1.16)$$

and, because $y(t)$ meet the differential equation (1.15),

$$y(t_{i+1}) = y(t_i) + hf(t_i, y(t_i)) + \frac{h^2}{2}y''(\xi_i) \quad (1.17)$$

Euler's method is built with approach $w_i \approx y(t_i)$ for $i = 1, 2, 3, \dots, N$, regardless of the last term found in equation (1.12). So the Euler method is expressed as :

$$y_0 = \alpha \quad (1.18)$$

$$y_{i+1} = y_i + hf(t_i, y_i) \quad (1.19)$$

The same is true for x , the euler method equation is used to calculate the value of the velocity derivative of the time entered into the program. Thus the euler method is expressed in equation (1.12) for the x and y fields. With constant constants: m_p, v_p, μ, π, η , dan R_p , and with constants dependent on (x, y) adalah $f(B/\mu(x, y))$, $B_x(x, y)$, $B_y(x, y)$, $\frac{B_x}{dx}$, $\frac{B_y}{dy}$. Next by specifying the euler method to find the value of, $\frac{dv_{p,x}}{dt} = f(B/\mu(x, y))$ or the x field, with the same step to find the value of $\frac{dv_{p,y}}{dt}$ in the y field.

Here the author makes a simulation to see the movement of drug particles in the human body because there is a magnetic field. The source of the magnetic field is derived from the wire. Researchers would like to see the magnetic field relationship of the wire flowing to the dynamics of drug particles in the human body. The purpose of this research is to make the dynamics model of magnetic particle particles of a nanometer-shaped particle in the human body using Euler method and to analyze the relation between distance and time to the determination of the speed of motion in the distribution of particle in the human body

2. METHODS

The tool used in this study is a set of computers with Windows operating system 10 with software program Matlab version R2016a. A solution of the differential equation (1.11) which describes the motion of nonmagnetic particles under the influence of magnetic field by using Euler method obtained by doing research procedure that is:

- Determination of magnetic field magnitude
 - The coordinate points x, y made using the meshgrid function.
 - The magnetic field value in two dimensions in the form of x and y .
 - The value of the magnetic field in the contour curve.
- Using the Euler method
 - The points in the distance of the equation (1.19)
 - The value of the velocity derivative of the time entered into the program using this method.

- Next by specifying the Euler method to find the value of velocity over time for the x, y fields.
- Numerical solution of particle drug dynamics
 - The solution of equation (1.17) can be expressed as the position of particles in the two-dimensional plane of the x-axis and the y-axis. The velocity value on the x-axis ($v_{p,x}$) or the first iteration is the input. The same thing is done for the y-axis ($v_{p,y}$).
 - Particle position, velocity is calculated recursively in time.

3. RESULTS AND DISCUSSIONS

3.1. Magnetic Field Distribution

This section describes the distribution of the magnetic field wire to the area around the body. On the magnetic field distribution on the magnetic field wire located in the area around the body. is determined by the coordinate points x, y made using the mesh grid function and then described the value of the magnetic field in the contour curve. Some things to be studied are the direction of the movement of particles around the magnetic field. Based on figure 1, the magnetic field strength distribution is in 2 coordinates (x and y). There are four magnetic field points and four contoured wires. The results show that the magnetic field has a region that is capable of attracting the existing adjacent particles to a place with a larger magnetic field. The closer to the magnetic field the particles will have high speed and vice versa. Although there are four magnetic field sources, the contour of the magnetic field near the wire is

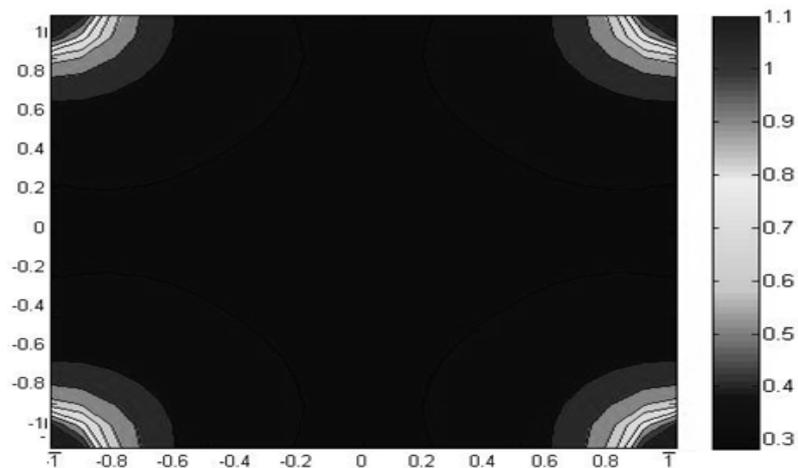


Figure 1: Distribution of a Magnetic Field with a Four-Wire Source Has a Current

Flowchart Simulation Program

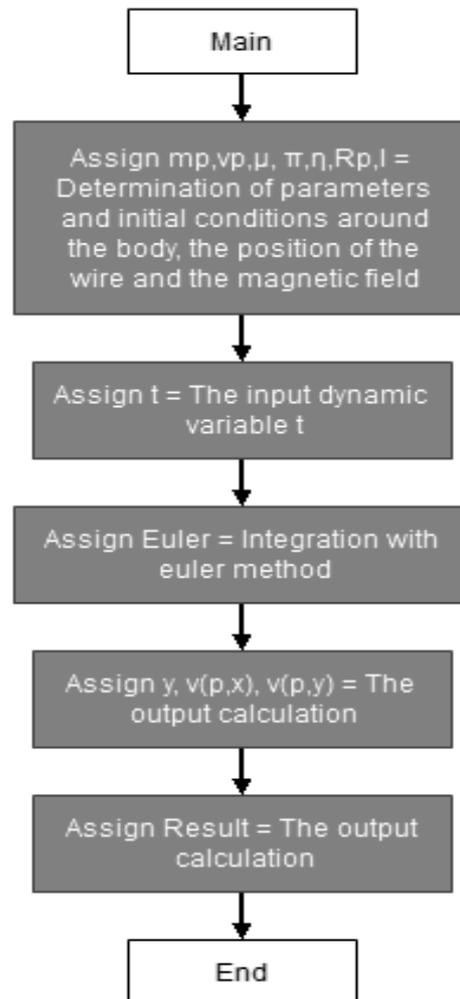


Figure 2

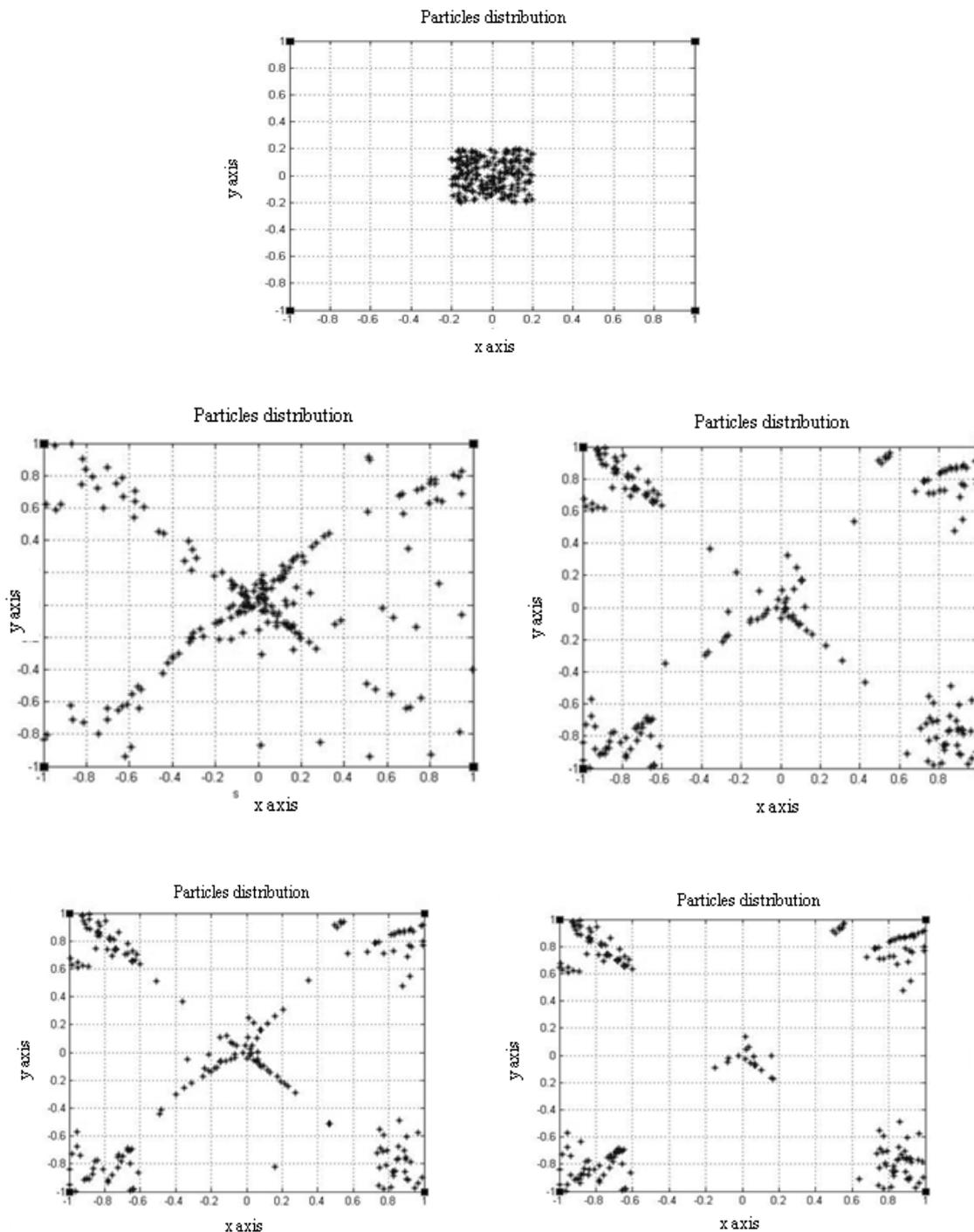
3.2. Numerical Solutions Dynamics of Particle Drugs

Differential equations solved by Euler method, calculating the value of the velocity derivative of the time entered into the program, the particles moving under the influence of the magnetic field are determined by the distance between the wires is 2 m

Particle positioning of the drug was randomized. The position of the wire is at the point (1,1) and (-1, -1) with the magnetic field distribution wire which is identical to the figure 1. In figure 2 the particles are at 0 seconds, with the initial state formed by the initial position (0.0). Particles of 200 particles will move closer to the four magnetic sources and are nearly symmetrically distributed across the four quadrants (I, II, III and IV)

Determination of the number of particles varied by 200 particles with the number of 100 iterations. The values of the variables dipassukkan into the program is the mass type 5000 kg.m^{-3} , saturation magnetization $M_{sp} = 4,78 \times 10^{-5} \text{ A.m}^{-1}$, and the viscosity of liquids $1,003 \times 10^{-3} \text{ N.s.m}^{-2}$

Some things to investigate are the direction of particle movement, particle velocity at each time, the position of the wire, and the strength of the magnetic field in two coordinate points (x and y), the maximum time the particle takes to the point of limit is 40 seconds.



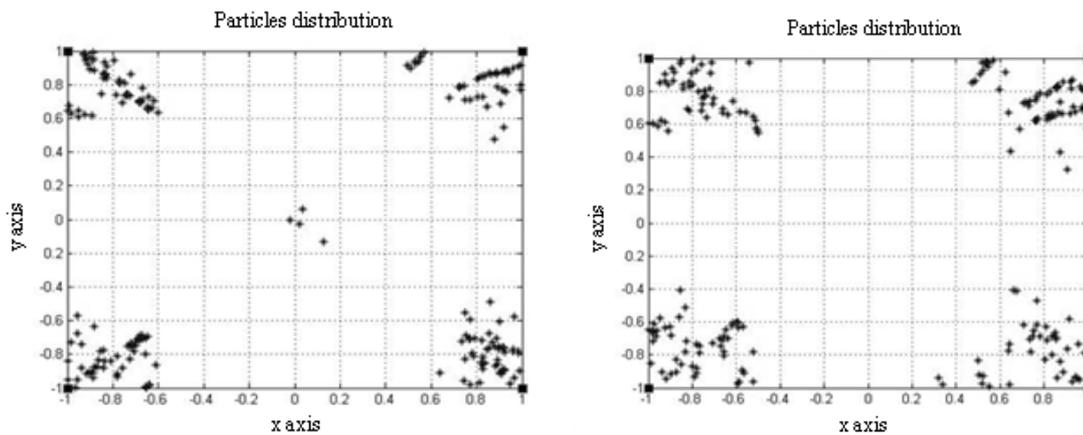


Figure 3: Distribution of Particles at 0 Seconds, 0.2 Seconds, 9.8 Seconds, 16.6 Seconds, 22.4 Seconds, 30.2 Seconds, and 40 Seconds

In figure 3 it appears that the particles at the starting point are still in a state of silence and have not experienced the movement. Particles have not been attracted to a larger magnetic field located at each end of the movement boundary.

The time of 0.2 seconds, the drug particles begin to move with particle position velocity calculated recursively with time. A number of particles distributed in quadrant I 12, 2%, quadrant II 12,9%, quadrant III 12,9% and quadrant IV 12,2%. The closer to the magnetic field, the particle will be attracted quickly toward the magnetic field with different speeds. Time 9.8 seconds of particles have been distributed in each magnetic field, the current used is 10 A and the magnetic field strength is 10 T. The particles are in quadrant I (15%), quadrant II (15.4%), quadrant III (15.4%) and quadrant IV (15%), the particles getting closer to the magnetic field movement will be faster. Time 16.6 seconds of the particles in quadrant I (19.2%), quadrant II (19.8%), quadrant III (19%) and quadrant IV (19%). Some particles are experiencing rapid movement and others experience slow movements. Time 22.4 seconds Participants in quadrant I (22.2%), quadrant II (22.8%), quadrant III (22%) and quadrant IV (22%), and unscattered particles 12%, and almost all particles are at the ends of the wire which is the source of the magnetic field. Time 30.2 seconds shows only four particles still moving slowly toward the magnetic field located at each end of the wire in 34 seconds, this caused because the speed of each particle is different because it is influenced by the position of B_x and B_y and almost all particles are in quadrants I, II, III, and IV, each of which is about 24% of 200 particles. Unlike when the particles were in the previous 25 seconds, where there are still particles that move slowly. At 40 seconds the particle's position is located at each end of the magnetic field within 40 seconds, the particles have been distributed in each quadrant, the closer to the magnetic field the particle will be more interested and the particles will move faster by using the formula in the equation (1.14) which has a magnetic

3.3. Particle Distribution on Field x

The particle distribution can be seen in figure 3. Particles of 200 particles are distributed in the planes of x and y, in the particle x plane of 200 particles divided into 21 points into 20 intervals, each interval distance of 0.1 m. This graph is obtained from 5 times the final particle position data

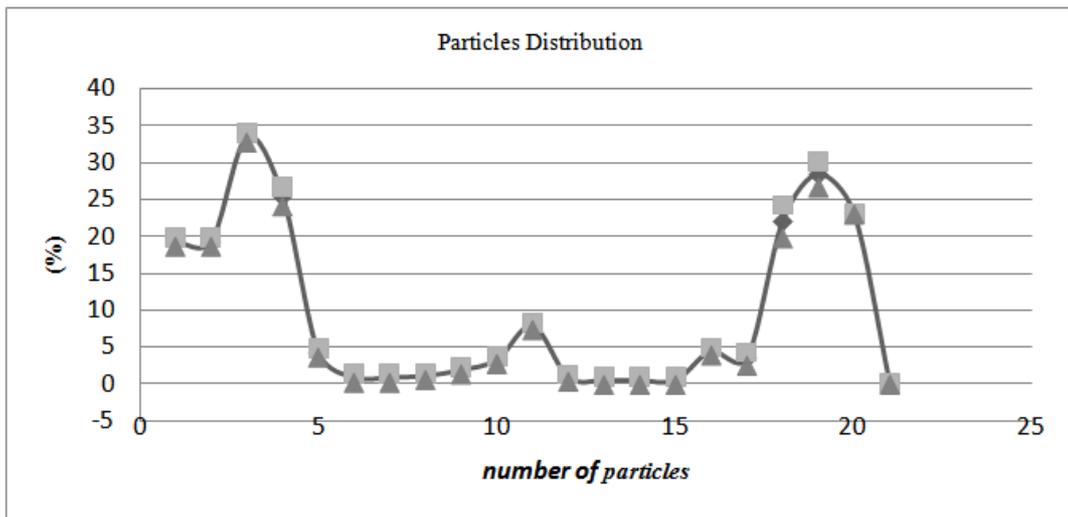


Figure 4: Graph of Particle Distribution for x Direction

In figure 4 it is seen from the interval 13-15 between the hoses (0.2- 0.5), has a small standard deviation whereas at interval 18 between the intervals (0.7-0.8) has a large standard deviation which has the maximum value and minimum value of each particle position. The more particles approaching the magnetic field the greater the particle velocity

3.4. The Relationship of Velocity with Time

As shown in figure 4, the graph shows the relationship between the average velocity of the particles to the function of time and the particle rate decrease exponentially appears that the particles move at maximum speed at 0.2 s, the maximum particle velocity is due to particle spacing which is getting closer to the source of the magnetic field

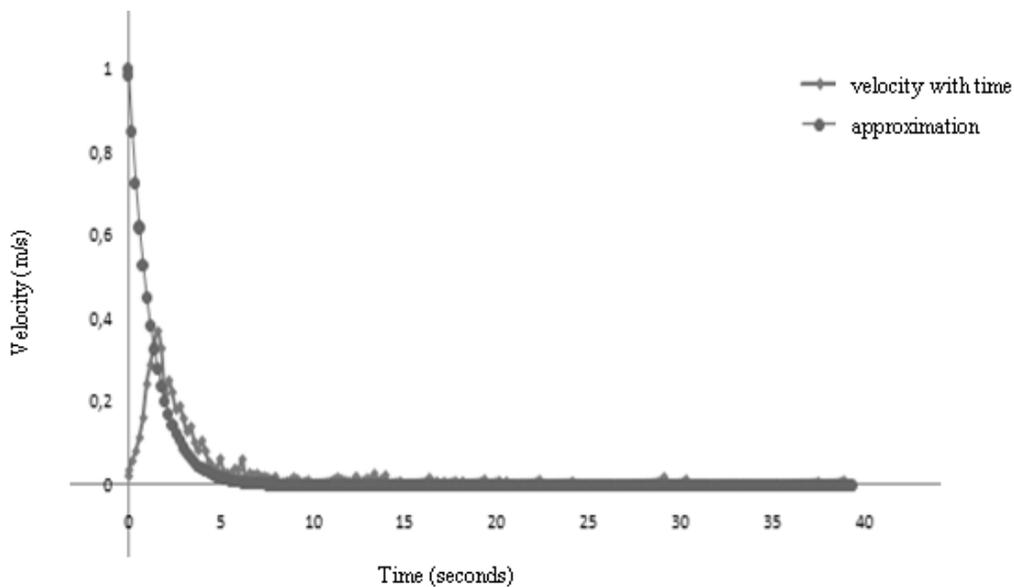


Figure 5: The Graph of the Average Velocity Relation at 0 Seconds to the Point 40 Seconds

When the particles pass through the position after the wire, the particle velocity, then decreases and tends to not move after the particles are already outside the source of the magnetic field. From the exponential approximation function used by the invisible method, it is concluded that for the approach function $f(t)=A \exp (-kt)$, the most approximant is if

$A=1$ dan $k=0,8$ with average velocity calculated $\frac{\Delta x}{\Delta t}$ s

To determine the position distribution of the final particles and made the grouping of particle positions in 20 intervals. The distribution of particles in the interval 13 to 15 corresponding to the hose (0.2-0.5), has a percentage of particle distribution of 1%. Particles in the interval 18 corresponding to the hose (0.7-0.8) have a percentage of particle distribution above 20%.

Particles that move at maximum speed at 0.35 seconds, particle velocity increases as particles move closer to the source of the magnetic field. By using the exponential function to predict the mean velocity of motion, it is concluded that for the function $f(t)= A \exp (-kt)$, the nearest value is $A = 1$ and $k = 0.8$

CONCLUSIONS

The calculation using the Euler method to solve differential equations in a magnetic drug simulation can be concluded that if the particle is closer to the source of the magnetic field, the faster the movement of the particle, the time it takes the particles to the magnetic field is 40 seconds. After that, the particles move slowly.

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REFERENCES

1. Alemzadeh, E., Dehshahri, A., Izadpanah, K., & Ahmadi, F. (2018). Plant virus nanoparticles: Novel and robust nanocarriers for drug delivery and imaging. *Colloids and Surfaces B: Biointerfaces*, 167, 20–27. <https://doi.org/10.1016/j.colsurfb.2018.03.026>
2. Babincova, M., & Babinec, P. (2009). MAGNETIC DRUG DELIVERY AND TARGETING : PRINCIPLES AND APPLICATIONS Melania Babincova, Peter Babinec. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub.*, 153(4), 243–250. <https://doi.org/10.5507/bp.2009.042>
3. Bautin, V. A., Seferyan, A. G., Nesmeyanov, M. S., & Usov, N. A. (2018). Properties of polycrystalline nanoparticles with uniaxial and cubic types of magnetic anisotropy of individual grains. *Journal of Magnetism and Magnetic Materials*, 460, 1–8. <https://doi.org/10.1016/j.jmmm.2018.04.019>
4. Bharali Marianne Khalil Mujgan Gurbuz Tessa M Simone Shaker A Mousa, D. J. (2009). Nanoparticles and cancer therapy: A concise review with emphasis on dendrimers. *International Journal of Nanomedicine*, 4, 1–7. <https://doi.org/10.2147/IJN.S4241>
5. Gawali, S. L., Barick, B. K., Barick, K. C., & Hassan, P. A. (2017). Effect of sugar alcohol on colloidal stabilization of magnetic nanoparticles for hyperthermia and drug delivery applications. *Journal of Alloys and Compounds*, 725, 800–806. <https://doi.org/10.1016/j.jallcom.2017.07.206>
6. Hoshidar, A. K., Le, T. A., Amin, F. U., Kim, M. O., & Yoon, J. (2017). Studies of aggregated nanoparticles steering during magnetic-guided drug delivery in the blood vessels. *Journal of Magnetism and Magnetic Materials*, 427(June 2016), 181–187. <https://doi.org/10.1016/j.jmmm.2016.11.016>

7. O'Donnell, M. (2018). Magnetic nanoparticles as contrast agents for molecular imaging in medicine. *Physica C: Superconductivity and Its Applications*, 548(March), 103–106. <https://doi.org/10.1016/j.physc.2018.02.031>
8. Rayegan, A., Allafchian, A., Abdolhosseini Sarsari, I., & Kameli, P. (2018). Synthesis and characterization of basil seed mucilage coated Fe₃O₄magnetic nanoparticles as a drug carrier for the controlled delivery of cephalexin. *International Journal of Biological Macromolecules*, 113, 317–328. <https://doi.org/10.1016/j.ijbiomac.2018.02.134>
9. Akinsola, Vo, And To Oluyo. "A Note On The Divergence Of The Numerical Solution Of The Mathematical Model For The Burden Of Diabetes And Its Complications Using Euler Method."
10. Yang, K., Son, J., Young, S., Yi, G., Yoo, J., Kim, D., & Koo, H. (2018). Biomaterials Optimized phospholipid-based nanoparticles for inner ear drug delivery and therapy. *Biomaterials*, 171, 133–143. <https://doi.org/10.1016/j.biomaterials.2018.04.038>

