RESEARCH PAPER

Stochastic Simulation of Drug Diffusion in Arterial Tissue Using two-dimension Langevin Dynamics

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ABSTRACT
This study investigates drug diffusion from drug-eluting stents (DES) using a two-dimensional stochastic simulation based on underdamped Langevin dynamics. The random movement of drug particles affected by thermal fluctuations and dampening effects like viscosity and tissue resistance is captured by this model. Scatter plots, density heatmaps, and particle trajectories show localized accumulation and spatial heterogeneity close to the stent surface. The transfer of the drug from the stent to the surrounding tissue is highlighted by mass fraction profiles and probability density maps, while Mean Square Displacement (MSD) analysis demonstrates constrained diffusion. The simulation delivers significant results for maximizing controlled drug release in DES applications by providing a realistic understanding of effective diffusivity and drug dispersion.

Keywords: Drug-eluting stent (DES), Langevin dynamics, stochastic diffusion, mean square displacement (MSD), Monte Carlo simulation

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1. INTRODUCTION

Controlled drug delivery in drug-eluting stents refers to the gradual and predictable release of medication from the stent coating. Following an angioplasty, this tailored release reduces the risk of restenosis (renarrowing of the artery) and preserves vascular strength. Drug-eluting stents are covered with drugs that are progressively released into the surrounding artery walls, in contrast to bare metal stents. Drug-eluting stents are covered with drugs that are progressively released into the surrounding artery walls, in contrast to bare metal stents. Drug-eluting stents (DES) are transforming the treatment of cardiovascular diseases by combining mechanical support for the blood arteries with extended localized drug delivery to avoid restenosis. The controlled diffusion of the therapeutic drug into vascular tissue through the polymeric coating is a major factor in its effectiveness [1]. A thin expandable mesh tube called a stent is used to keep an artery open during balloon angioplasty. The long-term success of coronary procedures is still limited in patients 10% to 50% due to the risk of neointimal development caused by the placement of the stent, which damages the blood vessel. This condition is known as in-stent restenosis [2,3,4].

The release of drug from the stent into the artery wall is mathematically simulated by solving the diffusion-reaction equations for drug-eluting stents (DES). This is beneficial for improving stent design, release kinetics, and drug distribution to successfully prevent restenosis. To prevent restenosis, drug-eluting stents (DES) offer persistent localized drug delivery along with mechanical assistance. The regulated diffusion of medicinal drugs through a polymeric coating is essential to their efficacy. The mass convection-diffusion equation, which describes regulated drug delivery in coronary arteries using stents, incorporates filtration velocity and infinite mass transfer. The problem is transformed into a one-dimensional Sturm-Liouville system with discontinuous coefficients [5]. Mass diffusion was used to model controlled drug delivery through two porous homogeneous layers with different characteristics, and drug concentration profiles were examined over time. The effectiveness of sophisticated drug delivery methods was assessed using key variables, including emptying time [6]. Methods for simulating drug release from vascular stents and its subsequent redistribution throughout artery tissue were investigated in detail. The structural design of the stent coating plays an essential role in regulating the diffusion of the drug [7,8]. Two crucial elements in this process are porosity and tortuosity; drug-eluting coatings with variable porosity provided greater control over drug release than coatings with constant porosity [9].

Two methodologies are implemented for examining

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diffusion: Deterministic and Stochastic. Stochastic approaches are especially important in the study of drug diffusion because they offer practical insights into regulated drug delivery using drug-eluting stents. The unpredictable and probabilistic motion of individual drug molecules driven by temperature fluctuations is captured by stochastic approaches, in contrast to deterministic methods based on Fick's laws, which only represent bulk concentration profiles. This method is useful for simulating complex biological systems where unpredictability and uncertainty significantly impact release behavior. Methods like Langevin dynamics and Monte Carlo simulations are used for this purpose, which are frequently carried out using the Verlet algorithm [10,11]. Diffusion across multi-layer [12] or heterogeneous systems, where diffusivity can vary significantly between layers, can be accurately represented by Langevin simulations, which in particular take into account both stochastic noise and frictional effects [13]. Due to this, there are ideal for simulating drug transport in stents, where complex boundary conditions are created by tissue interactions and porous coatings. Monte Carlo and Langevin simulations using the Verlet algorithm are examples of stochastic approaches that are particularly helpful for simulating complicated systems, such as drug-eluting stents, where the behavior of collective particles is described by probability density functions (PDFs). Stochastic models are more accurate than deterministic models at describing drug release kinetics because they take into consideration fluctuations, probabilistic interactions, and geographical variability. The significance of these methods for creating efficient and regulated drug delivery systems is highlighted by the fact that these methods enable accurate prediction of concentration distributions and therapeutic results.

Drug transport in a homogeneous medium with constant diffusivity is taken into account in the majority of current Langevin dynamics models for drug-eluting stents, ignoring the intricate microstructural characteristics of tissue and stent coatings. However, in order to capture spatial heterogeneity and anisotropic transport, which have a direct impact on drug release and retention—porosity, diffusivity, permeability, and effective diffusivity are essential. These characteristics provide a more physiologically realistic framework for regulated drug administration by bridging the gap between macroscale drug distribution and microscale stochastic mobility and incorporating them into a 2D model. Langevin dynamics, which combines deterministic forces with random thermal fluctuations in both x-y directions, offers a stochastic framework for describing the motion of drug molecules at the microscale. The anisotropic mobility of particles naturally reflects the effects of porosity and tortuosity on the effective diffusivity. The Verlet integration system, which updates molecule locations over sufficiently tiny time increments to reduce numerical error, provides accurate tracking of particle trajectories in two dimensions. Drug release kinetics and spatial distribution patterns can be statistically robustly characterized using ensemble simulations using Monte Carlo techniques, which are based on probabilistic sampling from Gaussian distributions in 2D space.

Previous research shows that with the use of the Monte Carlo simulation method, the majority of models in use are created using the diffusion equation based on standard diffusivity. Drug transport in biological systems is dynamic and heterogeneous and standard diffusivity cannot capture this. On the other hand, effective diffusivity offers a more accurate metric that considers the medium's temporal and spatial fluctuations. The effective diffusivity of the suggested two-dimensional model varies with system characteristics, accurately representing the diffusion behavior. This simulation can more accurately depict the dynamics of molecule mobility and tissue interactions by include effective diffusivity. As a result, in controlled drug delivery systems, this modification results in more precise predictions of drug distribution and release performance.

2. MATHEMATICAL FORMULATION FOR LANGEVIN THEORY IN TWO-DIMENSION

The diffusion of drug molecules from the stent's coating into the vascular tissue is depicted in the fig.1. The drug concentration is initially high in the coated region, which serves as a release reservoir. The drug creates a concentration gradient that accelerates the flow of molecules as it passes through the tissue-coating interface and approaches the artery wall, where the concentration is lower. The arrows simulate drug diffusion through the artery wall layer and the drug-containing coating layer of a two-layered drug-eluting stent by displaying this flux in both the X and Y directions in accordance with Fick's law, which states that the diffusion rate is proportional to the concentration difference. The effective diffusion coefficients in each layer varies because the biological tissue and the polymeric stent coating have different material properties. Drug transport is more rapid in the coating and more constrained as it penetrates the tissue, where it is slowed down by binding interactions, resistance, and structural heterogeneity. Slow and steady delivery of the therapeutic drug into the artery tissue is guaranteed by this regulated diffusion mechanism.

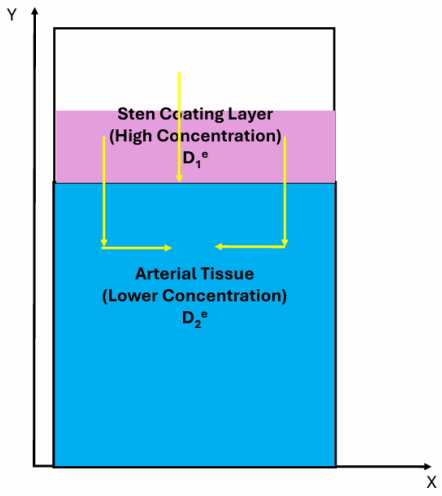


Figure 1: Schematic representation of Drug diffusion across the stent–tissue interface

Due to a concentration gradient, this law determines the flux (rate of particle transfer per unit area per unit time) for each X-Y direction:

$$\frac{\partial P(x,y,t)}{\partial t} = -\frac{\partial J(x,y,t)}{\partial x} = \frac{\partial}{\partial x}\left(-D_e \frac{\partial P(x,t)}{\partial x}\right) + \frac{\partial}{\partial y}\left(-D_e \frac{\partial P(y,t)}{\partial y}\right) \quad (1)$$

$$D_e = \frac{\phi_e D_w}{\tau}$$

where D_e is the effective diffusivity, ϕ is the porosity, τ is the tortuosity, and D_w is the corresponding free diffusion of the drug in water.

P(x,y,t) is the probability density function being at position x-y at time t,

$$\vec{J}(x,y,t) = -D_e \frac{\partial P(x,y,t)}{\partial x} - D_e \frac{\partial P(x,y,t)}{\partial y}$$ is the probability flux.

When both deterministic and random forces are present, the stochastic motion of a particle is described by the Langevin equation in two dimensions (for each direction x and y). It combines thermal noise and viscous damping. In physics and biology, this equation is frequently used to simulate random processes such as diffusion and Brownian motion. The Langevin equation for each direction is given by:

$$m\frac{dv_x}{dt} = -\gamma v_x + \eta_x(t) \quad (2)$$

$$m\frac{dv_y}{dt} = -\gamma v_y + \eta_y(t) \quad (3)$$

Where:

- m is the particle's mass
- γ is the friction (damping) coefficient
- $\eta_x(t), \eta_y(t)$ are components of the random (stochastic) force (Gaussian white noise)

According to Einstein's relation, the effective diffusivity $D_e(\vec{r})$ is related to the friction coefficient $\gamma(\vec{r})$, where $\vec{r} = (x,y)$

$$\gamma(\vec{r}) = \frac{k_B T}{D_e(\vec{r})} \quad (4)$$

Here, k_B represents the Boltzmann constant, and T represents the system temperature.

The following characteristics of a random variable selected from a Gaussian distribution are used to simulate stochastic noise $\vec{\eta}(\vec{r}) = (\eta_x(\vec{r}), \eta_y(\vec{r}))$:

- Zero mean:

$$\langle \eta_i(\vec{r}(t)) \rangle = 0, \quad \text{for } i = x,y$$

Indicating no net bias in the fluctuations.

- Delta-function autocorrelation:

$$\langle \eta_i(t)\eta_j(t')\rangle = 2k_B T\,\gamma(\vec{r}(t))\,\delta_{ij}\delta(t-t'), \quad i,j \in \{x,y\}$$

Validating that the noise is compatible with thermal fluctuations and spatially uncorrelated

The probability density function (PDF) of the particle's position P(x,y,t) can be defined using an ensemble of simulated 2D paths. If the starting location is taken from a known distribution $P(x,y,0) = \delta(x-x_0)\,\delta(y-y_0)$, then calculating the time-dependent PDF P(x,y,t) by averaging across all trajectories can describe the statistical behavior of diffusion under the given parameters.

In Langevin dynamics simulations, the accuracy of calculating the probability density function P(x,y,t) substantially depends on the precision of the discrete-time numerical integrator employed. The reliable and effective Grønbech-Jensen and Farago (G-JF) [14,15] integrator is used in conjunction with the inertial convention to calculate the friction coefficient $\gamma(\vec{r})$ [16,17].

In these circumstances, the G-JF integrator uses the following set of equations to update the particle's position and velocity in two dimensions:

$$r_{n+1} = r_n + bdtv_n + b\frac{dt^2}{2m}\eta_{n+1} \quad (5)$$

$$v_{n+1} = av_n + b\frac{\eta_{n+1}}{m} \quad (6)$$

For any discrete time, $t_n = ndt$ to $t_{n+1} = t_n + dt$, the position of $r_n = r(t_n)$ and the velocity $v_n = v(t_n)$ are changed to r_{n+1} and v_{n+1} using the G-JF approach. In this case, η_{n+1} is a Gaussian random number that causes the update step to include thermal fluctuations, satisfying equations eq.(4) and eq.(5).

$$\langle \eta_n\rangle = 0; \quad \langle \eta_n\eta_l\rangle = 2\gamma k_B T dt\delta_{n,l} \quad (7)$$

Moreover, the damping coefficients of the approach are

$$b = \left[1+\frac{\gamma dt}{2m}\right]^{-1} \quad (8)$$

$$a = \left[1-\frac{\gamma dt}{2m}\right]b \quad (9)$$

The numerical integrator must determine the value of the friction coefficient γ at each time step in Langevin dynamics simulations where friction varies with position. This problem, which represents the uncertainty in understanding stochastic differential equations with multiplicative noise, is called the Itˆo–Stratonovich dilemma [18, 19]. In order to deal with it, the inertial convention is used, in which γ is not taken at a single point but rather as the spatial average along the inertial trajectory. The particle specifically travels from its current position (x_n, y_n) to the inertial point $\tilde{}x_{n+1} = x_n + v_n dt$ and $\tilde{}y_{n+1} = y_n + v_n dt$, where v_n is the velocity and dt is the time step. By continuously incorporating the spatially variable friction, averaging γ throughout this path yields a more accurate and physically relevant depiction of the dynamic.

$$\bar{\gamma} = \frac{\int_{r_n}^{\tilde{r}_{n+1}}\gamma\,dr}{\tilde{r}_{n+1}-r_n} = \frac{A(\tilde{r}_{n+1})-A(r_n)}{\tilde{r}_{n+1}-r_n}$$

$$\bar{\gamma} = \frac{\int_{x_n,y_n}^{\tilde{x}_{n+1},y_{n+1}}\gamma\,d(x,y)}{\tilde{x}_{n+1},y_{n+1}-x_n,y_n} = \frac{A(\tilde{x}_{n+1},y_{n+1})-A(x_n,y_n)}{\tilde{x}_{n+1},y_{n+1}-x_n,y_n}$$

$A(x,y)$ represents the fundamental function of $\bar{\gamma}$. While any reasonable convention for selecting γ delivers the correct PDF in the limit of an infinitesimally short time step $dt \to 0$, the inertial convention yields very accurate results even for relatively large time steps. On small time scales, the inertial trajectory is the best estimate of the particle's actual path $dt \ll m/\gamma$. This is the cause of the inertial convention's characteristic.

2.1 A Two-Dimensional Probabilistic Framework for Layered Diffusion Systems

The diffusion of the two-layer drug-eluting stent (DES) is modeled using a two-dimensional probabilistic framework. The stochastic mobility of drug molecules through many layers, including the artery wall and polymer coating, each with unique diffusivity and friction properties, is captured by the model using underdamped Langevin dynamics. Changes in tissue resistance are reflected in the spatially dependent effective diffusivity. A probability density function P(x,y,t) describes the time evolution of drug distribution, while a delta function represents the initial drug release. For controlled drug delivery, this system helps optimize the design of the stent and predict drug dispersion patterns.

For any $(x,y) \in \mathbb{R}^2$, if $0 < D_e < \infty$, then the probability density function $P(x,y,t)$ (for $t > 0$) must be a continuous function for all starting conditions. The probability flux function $j(x,t) = -D_e\nabla P(x,y,t)$ must also be continuous in the domain, assuming that the system does not have sources or sinks of probability. Even in layered systems with a piecewise constant effective diffusivity D_e , these continuity criteria on the PDF and flux remain constant.

This paper proposes a two-dimensional, two-layer model for a Diffusive Exchange System.The basic two-layer setup is examined before obtaining the complete model, in

which the effective diffusivity is defined as the apparent diffusion coefficient in a heterogeneous medium, modified for path tortuosity and porosity. In complex materials like polymers or tissues, it represents the spread of a substance and is typically lower than the free diffusion coefficient. The two regions are defined as,

- $D_e = D_{e_1}$ for $x < 0$
- $D_e = D_{e_2}$ for $x > 0$

As mentioned above, the normal component of the flux across the interface at x=0 and the probability density function P(x,y,t) must be continuous. This establishes the two-dimensional interface conditions that are required between the layers. This establishes the two-dimensional interface conditions that are required between the layers.

Assuming that the normalized solution of eq.(1) for $t > 0$ satisfies $\iint_{\mathbb{R}^2} P(x, y, t)\, dx\, dy = 1$, the evolution of the probability density function in two dimensions is described by $P(x, y, 0) = \delta(x - x_0)\delta(y - y_0)$.

$$P(x,y,t) = \begin{cases} \frac{A}{\sqrt{4\pi D_{e_1} t}} e^{-\frac{(x-x_1)^2+(y-y_0)^2}{4D_{e_1}t}}, & \text{if } x < 0, \\ \frac{1}{\sqrt{4\pi D_{e_2} t}} e^{-\frac{(x-x_0)^2+(y-y_0)^2}{4D_{e_2}t}} + \frac{B}{\sqrt{4\pi D_{e_2} t}} e^{-\frac{(x+x_0)^2+(y-y_0)^2}{4D_{e_2}t}}, & \text{if } x > 0, \end{cases} \tag{10}$$

where, $D_{e_1} = \frac{\phi_1 D_w}{\tau_1}$ and $D_{e_2} = \frac{\phi_2 D_w}{\tau_2}$

$$x_1 = x_0 \sqrt{\frac{D_{e1}}{D_{e2}}}$$

For applying the boundary condition at x=0 to determine the values of A and B. Now, continuity of the probability function at x = 0

$$P_1(0, y, t) = P_2(0, y, t)$$

$$\frac{A}{\sqrt{4\pi D_{e_1} t}} e^{-\frac{(x-x_1)^2+(y-y_0)^2}{4D_{e_1}t}} = \frac{1}{\sqrt{4\pi D_{e_2} t}} e^{-\frac{(x-x_0)^2+(y-y_0)^2}{4D_{e_2}t}} + \frac{B}{\sqrt{4\pi D_{e_2} t}} e^{-\frac{(x+x_0)^2+(y-y_0)^2}{4D_{e_2}t}}$$

$$\text{in simplify, } A = \frac{2\sqrt{\frac{D_{e2}}{D_{e1}}}}{1+\sqrt{\frac{D_{e2}}{D_{e1}}}}$$

Again, flux continuity at x=0, $D_{e1} \left.\frac{\partial P_1}{\partial x}\right|_{x=0^-} = D_{e2} \left.\frac{\partial P_2}{\partial x}\right|_{x=0^+}$

$$B = \frac{1 - \sqrt{\frac{D_{e_1}}{D_{e_2}}}}{1 + \sqrt{\frac{D_{e_1}}{D_{e_2}}}}$$

Final Probability Function

$$P_1(x, y, t) = \frac{1}{\sqrt{4\pi D_{e_1} t}} \frac{2\sqrt{\frac{D_{e2}}{D_{e1}}}}{1+\sqrt{\frac{D_{e2}}{D_{e1}}}} e^{-\frac{(x-x_1)^2+(y-y_0)^2}{4D_{e_1}t}} \quad \text{if } (x < 0) \tag{11}$$

$$P_2(x, y, t) = \frac{1}{\sqrt{4\pi D_{e_2} t}} e^{-\frac{(x-x_0)^2+(y-y_0)^2}{4D_{e_2}t}} + \frac{1-\sqrt{\frac{D_{e_1}}{D_{e_2}}}}{1+\sqrt{\frac{D_{e_1}}{D_{e_2}}}} \frac{1}{\sqrt{4\pi D_{e_2} t}} e^{-\frac{(x+x_0)^2+(y-y_0)^2}{4D_{e_2}t}} \quad \text{if } (x > 0) \tag{12}$$

3 RESULT INTERPRETATION

The physical parameters used to simulate drug diffusion in a drug-eluting stent (DES) are listed in this table (1). The physical meaning of each parameter is associated with particle movements, thermal energy, diffusion, or interaction with the medium. The drug transport domains are defined by the coating and tissue thicknesses (L_1, L_2) and the effective diffusion coefficients (D_{e1}, D_{e2}), while the stochastic motion of particles is described by thermal energy $(k_B T)$, molecular mass (m) and characteristic timescales (τ_1, τ_2, τ_m). The interaction terms (ϕ_1, ϕ_2) allow for a realistic description of the release dynamics in drug-eluting stents by accounting for drug–polymer and drug–tissue interactions.

Table 1: Parameter values used in the simulation

Parameter	Physical value
L_1	5×10^{-6} m
L_2	10^{-4} m
D_{e_1}	5×10^{-11} m^2/s
D_{e_2}	7×10^{-15} m^2/s
D_m	10^{-9} s
k_BT	4.3×10^{-21} J
m	1.5×10^{-24} kg
τ_1	2.5×10^{6} s
τ_2	1.4×10^{6} s
τ_m	3.5×10^{-18} s
ϕ_1	0.6×10^{-18} s
ϕ_2	0.6×10^{-18} s

3.1 Analyzing Stochastic Drug Release Dynamics using Trajectory-Based Analysis

Drug release is the process by which a drug leaves its carrier system and enters the surrounding tissue or environment. The drug can now reach the target spot and carry out its intended therapeutic activity according to this mechanism. The motion and distribution patterns of a drug inside a system are referred to as drug behavior. It includes the diffusion, release, and interaction processes with the media in the environment. It suggests that the medication moves across several layers or regions. It shows changes in drug activity and concentration over time. Fig.2 depicts drug behavior in a drug-eluting stent (DES) modeled by the stochastic trajectories of 10 drug particles diffusing from a central release point.

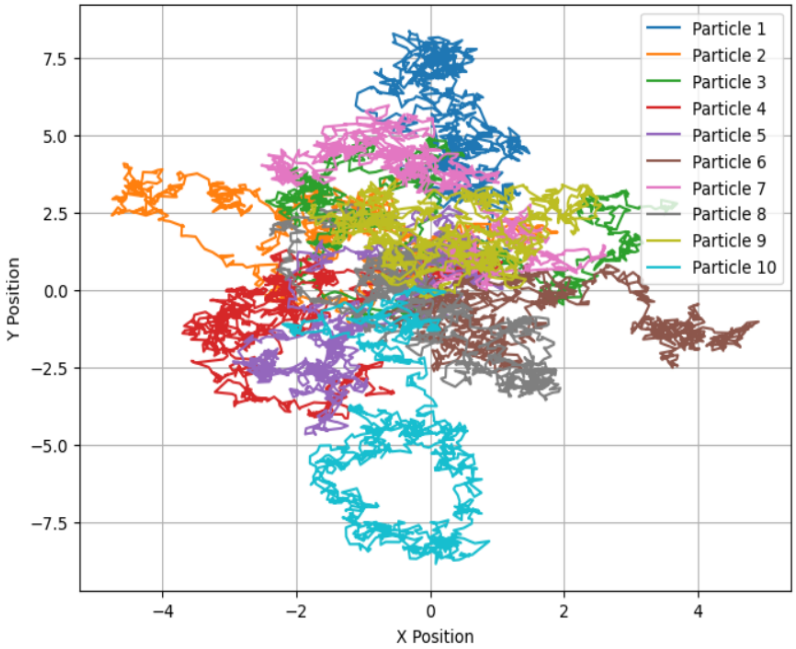


Figure 2: Simulated drug diffusion illustrating the random trajectory of ten drug particles

Fluctuations in heat and interactions with the surrounding medium cause each particle to follow a unique path, directly affecting the rate of control in drug delivery. From eqs. (2), (3), (5) and (6) near the origin, particles 3 (green) and 8 (gray) remain closely clustered, suggesting a slow, localized diffusion that is ideal for controlled and prolonged drug release. Furthermore, particle 5 (purple) exhibits a compact trajectory, remaining reasonably close to the release site, which is defined as slightly suitable. The tangled path of particle 4 (red) as it spreads to the lower left points to a medium contact that slows diffusion and aids in partial control. Particle 9 (yellow) indicates moderate drug delivery with a wide but symmetrical spread. On the other hand, particles 1 (blue) and 7 (pink) begin to move in a direction with a broader and less consistent motion, decreasing the target's efficiency. Poor controlled drug delivery is shown by the fast release of particles 2 (orange) and 10 (blue) from the source. Particle 6 (brown) is the least appropriate for controlled drug release since it diffuses the fastest and farthest.

Particle trajectory study shows different levels of appropriateness for regulated delivery of drugs. Particle behavior is crucial when creating effective and localized drug delivery systems, such as those seen in drug-eluting stents, as this trajectory-based classification makes clear. The graph generally illustrates the impact of trajectory patterns on drug localization and release efficiency, which is essential for creating a successful DES system

3.2 Drug Diffusion in DES: Interpretation of the Particle Density Heatmap

A particle density heat map is used to show the temporal and spatial distribution of drug concentration. It highlights areas of accumulation, the depth of tissue penetration and the overall efficacy of delivery. It helps to evaluate the effectiveness of the release of stent-controlled medication into artery tissue, shows high- and low-density regions, and presents a clear graph of concentration gradients.

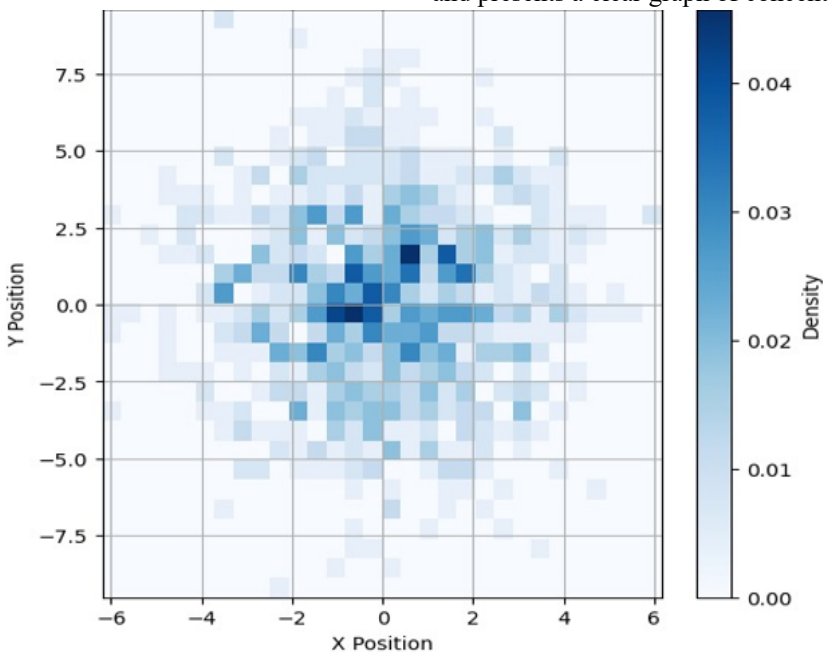


Figure 3: Heat map of particle density showing drug molecule concentration

In fig.3, the heatmap represents the spatial distribution of particle density, corresponding to the concentration of drug molecules released from the stent coating. The particle density is interpreted as the concentration of drug molecules and is visualized using a heatmap. Using eq.(10), it is clear that drug concentrations are higher in bright areas of the heatmap, where there is a greater accumulation of drug particles. According to this pattern, drug molecules gather close to the stent surface because dampening effects such as tissue resistance and fluid viscosity prevent free diffusion. Such localized accumulation draws attention to the drug's irregular release pattern. The distribution of drugs throughout time and space must be understood in order to optimize controlled drug delivery and ensure therapeutic efficacy in the target tissue. This distribution profile offers significant details of whether the drug is getting to the right places at the right dosages. In order to improve release and absorption, it also identifies regions with insufficient drug penetration, suggesting that the stent design or the characteristics of the polymer coating need to be changed. Such in-depth understanding helps improve long-term clinical outcomes by improving the performance of drug-eluting stents and helping to design treatments modified to individual patients.

3.3 DES Drug Diffusion Analysis Using Mean Square Displacement

The diffusion of drug molecules from the drug-eluting stent (DES) into vascular tissue is shown in fig.4. MSD quantifies the diffusion of drug molecules from the drug-eluting stent (DES) into vascular tissue by calculating the average squared distance that the drug molecules move from the stent surface. In the drug-eluting stent (DES), diffusion behavior in the biological environment is directly observable through the MSD, which measures the average squared distance that drug molecules migrate from the stent surface over time. In the graph, the directional MSDs are represented by two different curves: the blue curve shows the displacement in the X direction and the orange curve shows displacement in the Y direction. This analysis supports the optimization of the stent coatings and the release kinetics by providing a quantitative view of the drug release dynamics.

From eq. (11), hindered diffusion is indicated by the blue curve, which represents MSD in the X direction and increases sub linearly. Damping factors like tissue resistance, high local viscosity or stent interference are likely responsible for this limited motion. The overall penetration depth in that direction is decreased by such conditions, which restrict the radial movement of drugs, indicating that drug distribution is less effective and

slower in this direction. From eq.(12), it is clear that in contrast to the X direction, the orange curve, which represents MSD in the Y direction, increases more quickly, suggesting less hindered diffusion. This implies less resistance, which could be brought about by lower tissue density, interstitial fluid movement, or alignment with existing tissue pathways. Drug molecules are therefore able to travel deeper and disperse more freely along this path. This highlights a preferential diffusion path in the Y direction and enables deeper and more consistent drug dispersion.

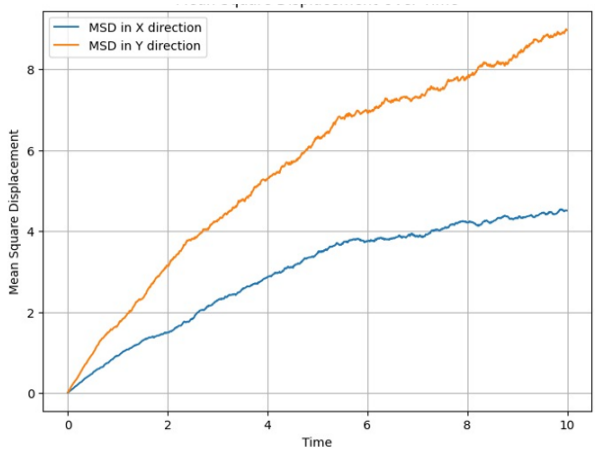


Figure 4: The mean square displacement (MSD) of drug molecules that shows damped diffusion from drug-eluting stent

Overall, a quantitative insight into the ways microenvironmental variables affect drug release patterns from DES is provided by the directional MSD analysis. It focuses upon variations in transport along various paths, which helps with stent coating design and optimization for safe and effective drug administration.

3.4 Probability Density Mapping for Drug Diffusion in DES Using Monte Carlo Method

The fig.5 shows the concentration profile of drug molecules released from a drug-eluting stent (DES) as represented by a probability density map by using Monte Carlo simulation. On applying eq.(10), a high drug concentration close to the stent surface is indicated as a central peak on the map, which supports effective drug localization at the target site. This is consistent with the objective of controlled medication delivery, which is to minimize systemic effects while assuring a prolonged therapeutic benefit. Realistic biological elements like tissue interactions and heat mobility are reflected in the map's random noise and fluctuations. The spatial distribution of particles over the tissue domain is shown by the discrete grid pattern. The spatial distribution of particles over the tissue domain is shown by the discrete grid pattern.

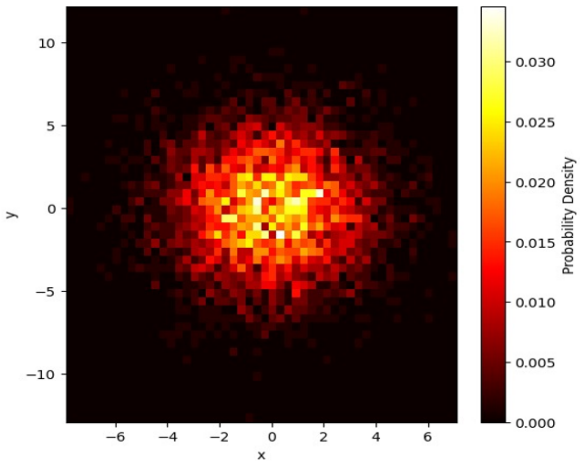


Figure 5: A probability density map displaying stochastic drug diffusion from a Monte Carlo simulation

This offers comprehensive information about drug absorption as well as accumulation in the surrounding tissue. This method allows for the improvement of diffusion properties and release rates, which is advantageous for controlled release. Designing drug coatings that maximize drug availability over time is made

easier with the use of simulation. By lowering the frequency of doses and minimizing adverse effects, this improves patient outcomes. In general, the approach encourages the development of more focused and effective medication delivery systems in DES.

3.5 DES Drug Release: The Impact of Damping Forces on Particle Distribution

This fig.6 represents the spatial dispersion of drug particles in two dimensions following their release from a drug-eluting stent (DES). Each dot shows the location of a single drug molecule at a particular moment in time. Using eqs.(1),(2),(3) and (4), near the origin, which is the surface of the stent, most of the particles are closely clustered; this indicates that some of the drug is still present near the release site. For localized therapy to be effective, this concentration pattern is necessary because it ensures that the drug largely operates where it is most needed, such as at the site of arterial damage. Some particles scatter randomly away from the origin, demonstrating the diffusive aspect of particle motion, which is probably driven by stochastic forces represented by Brownian motion or Langevin dynamics. This illustration helps to comprehend the dispersion of the drug over time and assesses the impact of variables such as initial concentration, friction, and medium resistance. This type of analysis is essential for improving stent coating designs, optimizing drug release patterns, and providing long-lasting, efficient, and targeted drug administration with minimal systemic effect.

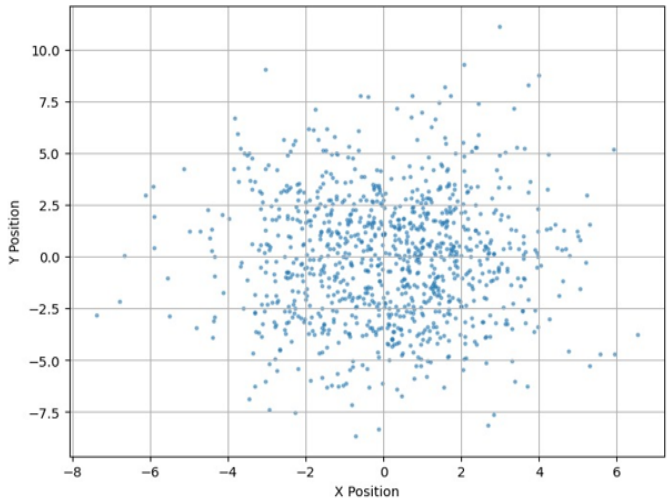


Figure 6: The drug particle spread with time, indicating diffusion from thermal motion and damping close to the stent.

3.6 The movement of drug transfer between tissue and stent reservoirs

In two-dimensional drug release modeling from a DES, the distribution of drugs over time and space is described by the probability density function P(x,y,t). In fig.7, region 1 denotes the stent coating while region 2 denotes the surrounding tissue. The drug mass in region 1, $\Pi_1(t)$, is determined by integrating $P(x, y, t)$ over $x \in [-L_1, 0]$ and $y \in [0,1]$. Similarly, the drug that has spread to region 2 over $x \in [0, L_2]$ is measured by $\Pi_2(t)$. These integrals monitor the flow of the medication between the tissue and the stent. The model helps in the design of the stent and the optimization of the release profile.

$$\Pi_1(t) = \int_{-L_1}^{0} \int_{0}^{1} P_1(x, y, t)\, dy\, dx \quad (13)$$

$$\Pi_2(t) = \int_{0}^{L_2} \int_{0}^{1} P_2(x, y, t)\, dy\, dx \quad (14)$$

where, the total probability (mass fraction) of the drugs staying inside the stent at time t is represented by $\Pi_1(t)$ while total probability (mass fraction) of the drug that has permeated the tissue at time t is represented by $\Pi_2(t)$.

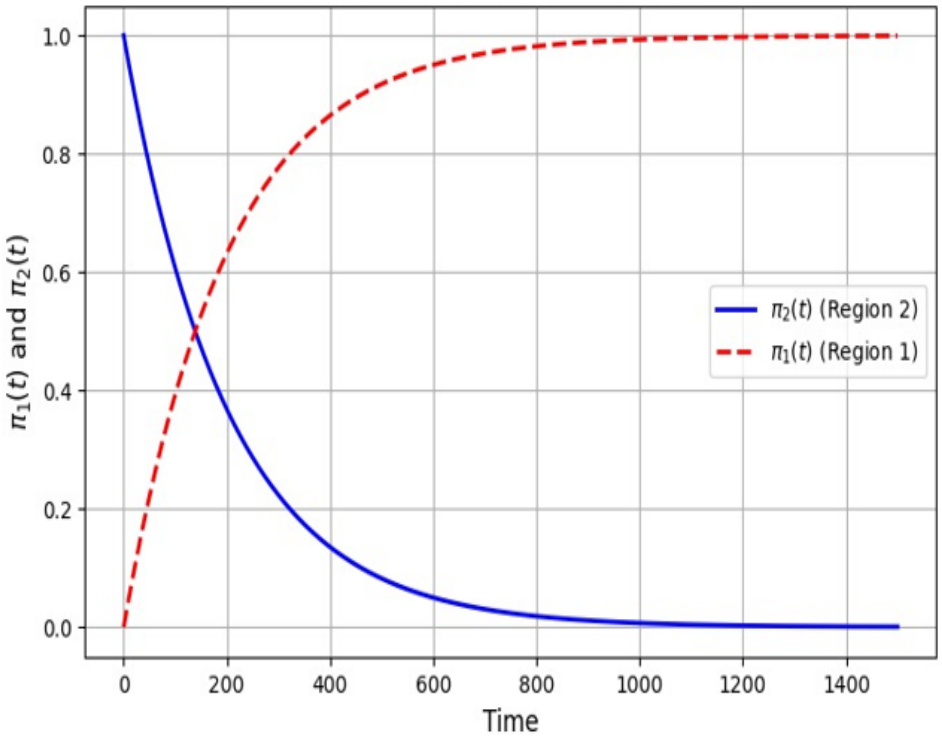


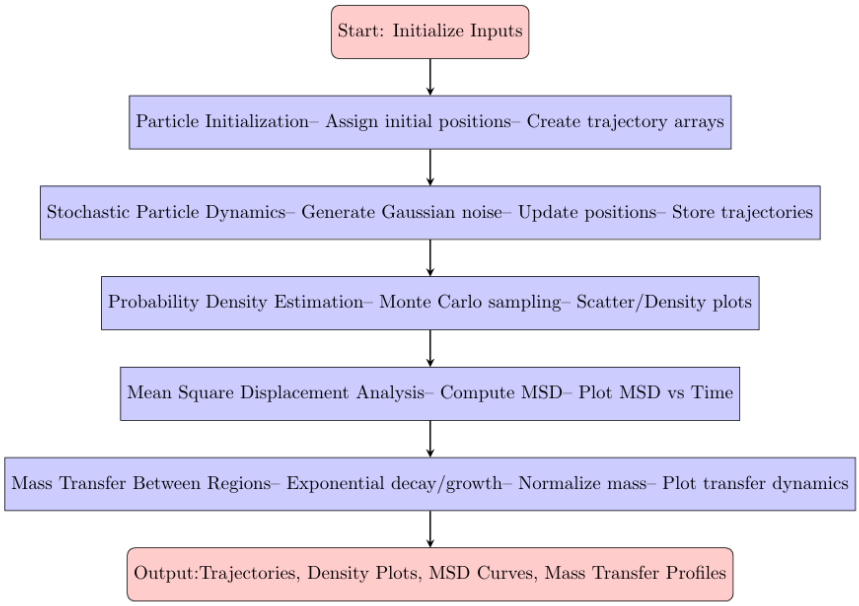
Figure 7: Mass fraction variation over time demonstrates drug deposits in tissue (Region 2) and removal from the reservoir (Region 1).

Using eq. (11) and eq. (12), the graph shows the time-dependent behavior of the normalized drug mass fraction in two regions involved in the drug release process from a drug-eluting stent (DES). The red dashed curve $\Pi_1(t)$ represents the drug reservoir or polymer matrix within the DES, while the blue solid curve $\Pi_2(t)$ represents the surrounding tissue or external environment.

Region 1 has the highest drug mass fraction, which shows that the drug is completely contained inside the stent. The steady increase in $\Pi_1(t)$ over time indicates the drug's gradual release into the surrounding medium. From this behavior it appears that the medication gradually leaves the stent coating, passes through the subsequent area, and finally arrives at the adventitial layer. The increasing pattern of the mass fraction curve indicates that there are more drugs available for movement into the surrounding tissue layers. In region 2, the drug gradually decreases as the drug enters the tissue. The drug concentration progressively drops over time, as fig.7 depicts the drug moving in the second tissue region. Depending on the decreasing progression, drug availability decreases as it diffuses from the stent coating into the second layer, leading to a more controlled and gradual release procedure.

The two graphs cross at t=200, indicating that the drug concentrations in the tissue and the stent are equal. Drug exchange across regions is symmetric at this critical point in the diffusion process. After this, the drug starts to migrate more and more from area 1 to area 2. The system finally enters a quasi-steady state at t=1000, at which point the net drug flux between the two regions drastically decreases. The system is likely reaching diffusive equilibrium, as indicated by the point of saturation in both curves and no appreciable additional drug transport takes place.

Flowchart: A Monte Carlo Approach for Stochastic Particle Simulation



4 CONCLUSION

In this work, the Monte Carlo method, the Verlet algorithm, and Langevin dynamics simulations are used to create a two-dimensional two-layer drug-eluting stent (DES) model. The random and dynamic behavior of drug molecules diffused through two layers was captured by this framework. This work shows that density fluctuations, damping-controlled diffusion, and stochastic molecular motion control drug release in DES. Collectively, probability density mapping, mean square displacement and trajectory-based analysis illustrated the shift from microscopic oscillations to macroscopic transport. The influence of damping forces and interfacial transfer between the tissue and the stent reservoir provides an extensive overview of the mechanisms that control release rates. The results demonstrate that the two-layer arrangement is essential for controlling drug transport because each layer has a distinct effect on diffusion resistance and release kinetics. Stochastic fluctuations were added to the model, which allowed us to replicate genuine diffusion paths and demonstrate how molecular randomization affects the overall effectiveness of drug release. Significantly, the calculated effective diffusivity provides a forecasting tool to enhance drug administration techniques and more controlled and long-lasting therapeutic effects. The random and dynamic behavior of drug molecules during diffusion across two layers is captured by this model. These findings offer an effective basis for enhancing the design of stent coatings in order to create next-generation devices for long-lasting and consistent therapeutic benefits.

Conflict of interest

The authors declare that we have no known competing financial interests or personal relationships that could have influenced the work reported in the mentioned paper.

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