

Deep-Learning Augmented PDE Models for Cellular Metabolic Regulation: An Integrative Biochemistry–AI Approach

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ABSTRACT

By combining basic biochemical laws with advanced AI-based learning, PDE models with deep learning have become an effective way to describe the multiscale dynamics of cellular metabolic regulation. The primary aim of this study is to develop an AI-enhanced biochemistry model capable of identifying metabolic phenomena that are either obscured or overlooked by conventional PDE models. The method has two parts for preprocessing: one that utilises deep learning to get features and another that employs statistical cleaning, normalisation, and stratification. Then, a GLM core that has been improved using Mantel-Haenszel stratified analysis to account for confounding effects is used to build the model. A hybrid deep learning architecture and a fusion module based on transformers are utilised to combine distinct biological inputs and learn patterns based on both partial differential equations (PDEs) and data. The results demonstrate a big improvement in computational efficiency, with a runtime that is about 26.7% faster, a cost that is about 18% cheaper, and a predictive performance that is around 0.91 AUC and 0.88 F1-score. The log-binomial model has the greatest accuracy (93%). The results indicate that PDE frameworks using deep learning provide a high-performance, interpretable, and scalable method for characterising metabolic rewiring, which is advantageous for metabolic engineering and precision biology.

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1. Introduction

The study of metabolic processes inside cells is essential in biochemistry. All living things are made up of metabolic processes. Traditional modelling approaches might still fail horribly when it comes to the complicated processes that happen in cells. The laws of reaction kinetics and transport, which are mostly described by Partial Differential Equations (PDEs), regulate most of the changes in metabolite concentration within a cell. Nonetheless, while their biophysical underpinnings, purely mechanistic PDE models encounter significant obstacles in accurately delineating intracellular environments, characterised by many unknown variables and the neglect of molecular interactions. The growing subject of integrative biochemistry–AI, which combines the predictive capabilities of Deep Learning with full mechanistic PDE frameworks, solves this problem. This new technique that adds a neural network to the PDE framework is also called a physics-informed or deep learning-augmented PDE model. Using this strategy, the AI can directly learn "latent" physical principles from high-dimensional omics data, such as unknown response rate laws or spatial transport dynamics. These ideas could be hard to understand or not complete. This approach makes sure that the taught parts are in line with known physical laws by following the structure of the PDE. This makes the model more accurate and better at making predictions while still being easy to understand physically. This approach looks to see whether the physical laws fit up with the things that have been taught. With this method, scientists can learn more about how cells react to outside signals by changing how they use energy. This understanding has important effects on precision medicine, drug discovery, and metabolic

engineering.

In order to adapt to new information, nutrients, and stimuli from the outside world, cells are constantly reorganising their internal metabolic processes (Gomes & Blenis, 2015). Cells can keep their balance, make more energy, and meet their biosynthetic demands for growth and repair within the cell thanks to these changes. Metabolic rewiring is a frequent way for cells to adapt and stay alive. For example, yeast cells are responsible for responding to changes in the availability of nutrients (Moxley et al., 2009), as well as in the cells of multicellular creatures during development (Miyazawa & Aulehla, 2018), sickness (Chapman & Chi, 2022), or environmental stress (Sengupta et al., 2011).

Metabolic rewiring alters the biochemical makeup of cells, and the alterations seen in the intracellular metabolome provide insight into the fundamental cellular adaptability (Schmidt et al., 2021). Conventional techniques in metabolomics are categorised as either targeted or untargeted. Targeted metabolomics concentrates on a specific group of metabolites of interest, confirmed within the observable chemicals; it seeks to correctly identify and quantify this predetermined set of metabolites, but can overlook new or unexpected ones (Lu et al., 2017; Wieder et al., 2021). Untargeted metabolomics facilitates an exhaustive analysis of all identifiable metabolites in a biological sample; nonetheless, it has obstacles related to reproducibility, the identification of unknown chemicals, and the development of a sensitive approach for all pertinent substances (Dunn et al., 2013; Xavier, 2024). Recent advancements in data-driven biomedical research highlight the growing importance of integrating multi-omics analysis, machine learning, and clinical insights to better understand complex disease mechanisms and improve healthcare outcomes (Othman et al., 2025). In cancer and immunological studies, bioactive compounds and oxidative stress regulation have been increasingly recognized for their therapeutic potential and role in disease progression. Additionally, lifestyle and clinical factors such as physical activity, sleep behavior, and healthcare practices contribute significantly to patient outcomes and disease management (Momani et al., 2025). The application of advanced machine learning techniques, including deep learning models for disease classification and predictive analytics, has further enhanced diagnostic accuracy and computational efficiency in modern healthcare systems. Collectively, these interdisciplinary approaches provide a comprehensive foundation for developing intelligent, data-driven, and personalized healthcare solutions.

It is well recognized that machine learning in science and engineering faces challenges due to the restricted availability of data. Conducting experiments to demonstrate this can be costly and time-intensive, and some values are difficult or unfeasible to quantify using existing methodologies. Likewise, high-fidelity numerical simulations are computationally expensive or potentially impractical for several applications. To mitigate over fitting in relatively short datasets, our method utilizes a priori known and represent able physics by integrating a deep neural network $h_\theta(u, v, w)$ inside a PDE framework that encapsulates the known and represented physics. This produces the category of PDE models:

$$\frac{\partial u}{\partial t}(t, x) = \underbrace{f_v(u(t, x), u_x(t, x), u_{xx}(t, x))}_{\text{known and represented physics}} + \underbrace{h_\theta(u(t, x), u_x(t, x), u_{xx}(t, x))}_{\text{Unknown / represented physics}}, \quad (1.1)$$

Where $u(t, x) = (u_x(t, x), \dots, u_d(t, x)) \in \mathbb{R}^d$, $x = (x_1, \dots, x_q) \in \mathbb{R}^q$, $u_x(t, x) = (u_{1,x}(t, x), \dots, u_{d,x}(t, x)) \in \mathbb{R}^{d \times q}$, and $u_{xx}(t, x) = (u_{1,x_1x_1}(t, x), \dots, u_{1,x_qx_q}(t, x), \dots, u_{d,x_1x_1}(t, x), \dots, u_{d,x_qx_q}(t, x)) \in \mathbb{R}^{d \times q}$. The term $f_v: \mathbb{R}^{(2q+1)d} \rightarrow \mathbb{R}^d$ represents the established physics in the PDE, with v representing the physical and contextual characteristics that delineate the application. The generalisation to include mixed second-order and higher-order derivatives is simple. Suitable beginning and boundary conditions fully specify the PDE. The neural network $h_\theta: \mathbb{R}^{(2q+1)d} \rightarrow \mathbb{R}^d$ will acquire the ability to characterise the unknown or unrepresented physics (as specified more accurately below) via the neural network parameters $\theta \in \mathbb{R}^{d\theta}$, which are derived from data analysis. In the turbulence simulation application under consideration, there are three components of u , therefore $d = 3$, and three spatial dimensions, thus $q = 3$.

There are expected to be two types of unrepresented or unknown physics. In the first, solving the governing equations would be prohibitively costly in terms of computing. Deep learning can be used to create a simplified model in this situation. In order to simulate the physical impacts of tiny unresolved turbulence scales on the larger scales represented by the large-eddy simulation (LES), the simplified model for the Navier-Stokes turbulence example that we analyse incorporates a sub-grid scale stress closure. In the second scenario, crucial physics is left out, either because it is thought to be too expensive (multi-component diffusion in reactive flows, for instance) or because it is really unknown. Generally speaking, the accuracy of the PDE model will be reduced by unrepresented or unknown physics. The chosen PDE model can serve as a foundation for the creation of machine learning models in both situations since it is only lacking and not flawed. The purpose of the suggested deep learning formulation is to enhance these governing equations using more, although constrained, high-fidelity simulation or experimental data.

It is expected that because to their extensive success, deep neural networks would be proficient in this role; hence, (1.1) is classified as a deep learning PDE model (DPM), but the overarching methodology would be applicable to any

comparably trainable machine learning framework. The model parameters θ are derived using reliable data $V(t, x; v)$, which are presumed to be accessible at certain periods $t_1, \dots, t_{N_t}$ and for particular physical or scenario parameters $v_1, \dots, v_M$. Specific V will be presented for certain demos thereafter. These are used to quantitatively approximate a neural network h_θ that, as shown in (1.1), produces the solution u that most accurately aligns with the reliable data V . This is accomplished by minimising the goal function.

$$L(\theta) = \sum_{m=1}^M \sum_{n=1}^{N_t} \int_{\Omega} \|u(t_n, x; v_m) - V(t_n, x; v_m)\| m(dx), \quad (1.2)$$

where the notation $u(t, x; v)$ directly denotes the dependency of u on v . The measure $m(dx)$ equals (dx) if the whole of Ω is used for training, however this is not necessary. For instance, $m(dx) = 1_{x \in \Omega_L} dx$ signifies that only data inside $\Omega_L \subset \Omega$ is used (Ghosal, 1996).

Deep Learning (DL), a prevalent and rapidly advancing technology, underpins several facets of contemporary civilisation and has significantly enhanced the state-of-the-art in computer vision, data mining, and natural language processing, among other fields (LeCun et al., 2015). Deep learning seeks to identify and understand complex structures within data by training computer models composed of several processing layers, enabling the acquisition of data representations at various levels of abstraction. In addition to conventional Artificial Intelligence (AI) and Machine Learning (ML) tasks, such as speech recognition and object detection, recent advancements in Deep Learning (DL) have begun to investigate the intersections of various disciplines, including applied mathematics, dynamic systems and Scientific Computing (SC) (Raissi et al., 2020), (Yadav et al., 2015). Historically, research in SC has mostly focused on issues with well-defined processes, such as modelling and prediction using various physical models (Heath, 2018). Over time, this strategy has evolved into a recognised disposal technique: using instruments like as Differential Equations (DEs) for descriptive and effective mathematical modelling of processes, and implementing efficient algorithms for their resolution (Dahlquist & Björck, 2008). Thus, precise outcomes can be achieved without dependence on extensive data or only a little dataset. Conversely, data-driven AI computation can get approximation answers without understanding the underlying process. Consequently, it has gained significant value in the current age of data and computational power proliferation by supplying enough data and efficient features to train various feature-centric models, including Artificial Neural Networks (ANNs) in machine learning.

In South Carolina, differential equations are regarded as useful for elucidating many scientific issues and technical contexts (Golub & Ortega, 1992). Ordinary Differential Equations (ODEs) and Partial Differential Equations (PDEs) provide the basis for this system, which consists of first- or higher-order derivatives of unknown functions with one or more variables (Farlow, 2006). The goal of this method is to find the derivatives of unknown functions using an equation, rather than using the algebraic formulas used in basic algebra. Therefore, functions that satisfy the connection should be its solutions. When it comes to real-world applications, DEs are the backbone of depicting complex processes in the social and natural sciences. For example, stochastic PDEs are used to tell statistical inferences about random processes, and dynamic systems are often used to describe the relationship between states in physical (Soldatenko & Yusupov, 2017) and financial issues (Chen, 2008; Rodkina & Kelly, 2011).

Direct training of DNNs using PDEs is a common feature of these methods. Constraints in many real-world applications are often imposed during model training as a loss function by use of generalised prior knowledge (GPR) in the form of DEs (Lu, Meng, et al., 2021). This approach was first suggested in the late 80s and refined in the 90s by Lagaris et al. (1998). Recently, Raissi et al. (2019) planned the renowned derivative known as PINNs, which demonstrated the capabilities of this technique across several contexts (Jagtap et al., 2020; Meng & Karniadakis, 2020; Zhang et al., 2019).

DL libraries have also been built for solving DEs, such as DeepXDE. The use of partial differential equations (PDEs) as training constraints relies on the premise that multilayer feedforward neural networks (FFNNs) can operate as universal approximators for high-dimensional functions (Hornik et al., 1989). Both training deep neural networks and solving differential equations aim to achieve optimal approximations. In other words, whether it is the Finite Element Method (FEM) employing basis functions to approximate the accurate solution in a unit or Deep Neural Networks (DNNs) utilising a complex architecture to model high-dimensional functions, the computed or predicted values at each unit centre or sampling point must converge infinitely towards the actual value (Momani et al., 2025; Othman et al., 2025). In DNNs, the loss function value, referred to as the residual, should ideally approach zero, whereas in numerical methods, it represents the computational error of the solution. Initially, such techniques were referred to as soft constraints, since the previous information represented by PDEs just constrains the accuracy of the projected outcomes without directing the optimisation process. The use of PDEs as constraints is often used to represent certain circumstances (Lu, Pestourie, et al., 2021). For instance, the Physics-Informed (PI) deep learning approaches have effectively been used to resolve the Navier-Stokes equations, as seen in Figure 2. Moreover, additional constraints in the form of initial and boundary conditions (ICs/BCs) are considered throughout the modelling process.

Given that the constraints derived from PDEs are often continuous inside the research domain, the training of DNNs does not rely on discretised grids as traditional numerical approaches do, hence achieving excellent accuracy (Cuomo et al., 2022). Furthermore, integrating posterior knowledge from measured data into constraint or loss functions can provide an improved solution (Raissi & Karniadakis, 2018). However, changes in physical parameters, coefficients, or initial conditions/boundary conditions would result in distinct limitations. The deficiencies are therefore evident due to the re-optimization of DNNs for various contexts.

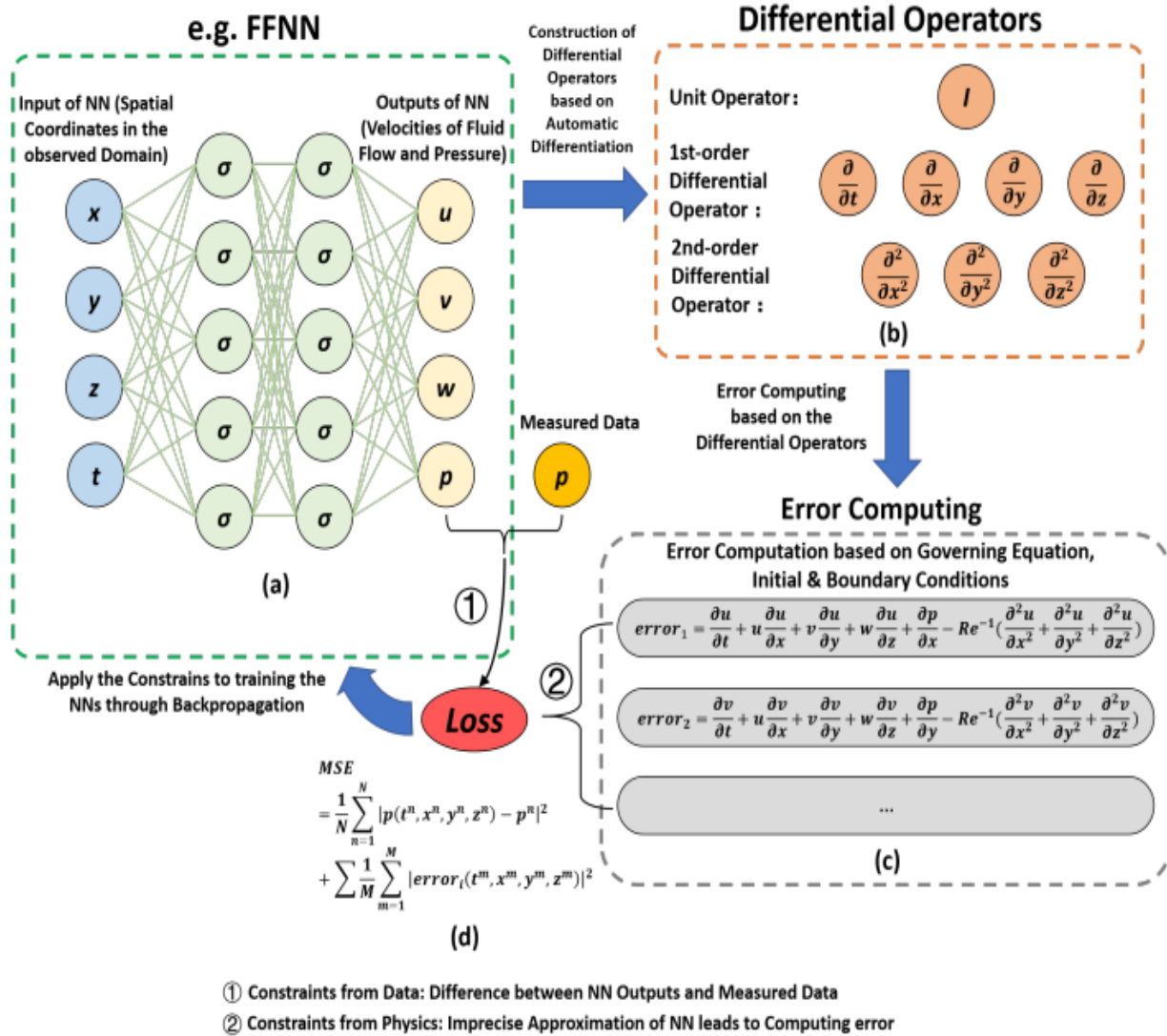


Figure 1: Schematic Representation of the Physics-Informed Neural Networks (PINNs) and its Use in Solving the Navier-Stokes Equations: (a) The Utilised Feed-Forward Neural Networks to Achieve the Approximation Aims; (b) and (c) Differential Operators Serve As Elements For Constructing The Error Computation Based On Partial Differential Equations, Representing the Limits Imposed by Various Physical Laws; (d) Incorporated Loss Function of Physical Limitations and Empirical Data to Train Neural Networks Using Backpropagation (Huang et al., 2025).

A unique method for intelligent numerical computation, using a Multi-Layer Perceptron (MLP) feed-forward back-propagation Artificial Neural Network (ANN) based on the Levenberg-Marquardt algorithm. The data collection was performed to enable the assessment, verification, and training of the artificial neural network model. The numerical results are clearly shown for various restrictions of the governing parameters. The elevated velocity ratio augmented the fluid velocity asserted by Reddy et al. (2025). Whereas, a technique using deep neural networks to estimate the spectrum transmittance of all-optical switches. The results confirm the effectiveness of deep learning in the development of all-optical plasmonic switches, recognised as the fastest switches at the nanoscale. The nonlinear Kerr effect in square resonators is used to illustrate the switching performance explained by Adibnia et al. (2024). On the other hand, the electronic structure characteristics of adsorbates can resolve this issue, diverging from the conventional design of substrate electronic structure

features prevalent in catalysis literature. This research reinforces the transferability attributes of SAAs and demonstrates that adsorbate-based electronic structure features, derived from either relaxed or unrelaxed chemical datasets, are effective instruments for predicting catalytic binding energies in these systems demonstrated by Shirani et al. (2024).

2. Research Methodology

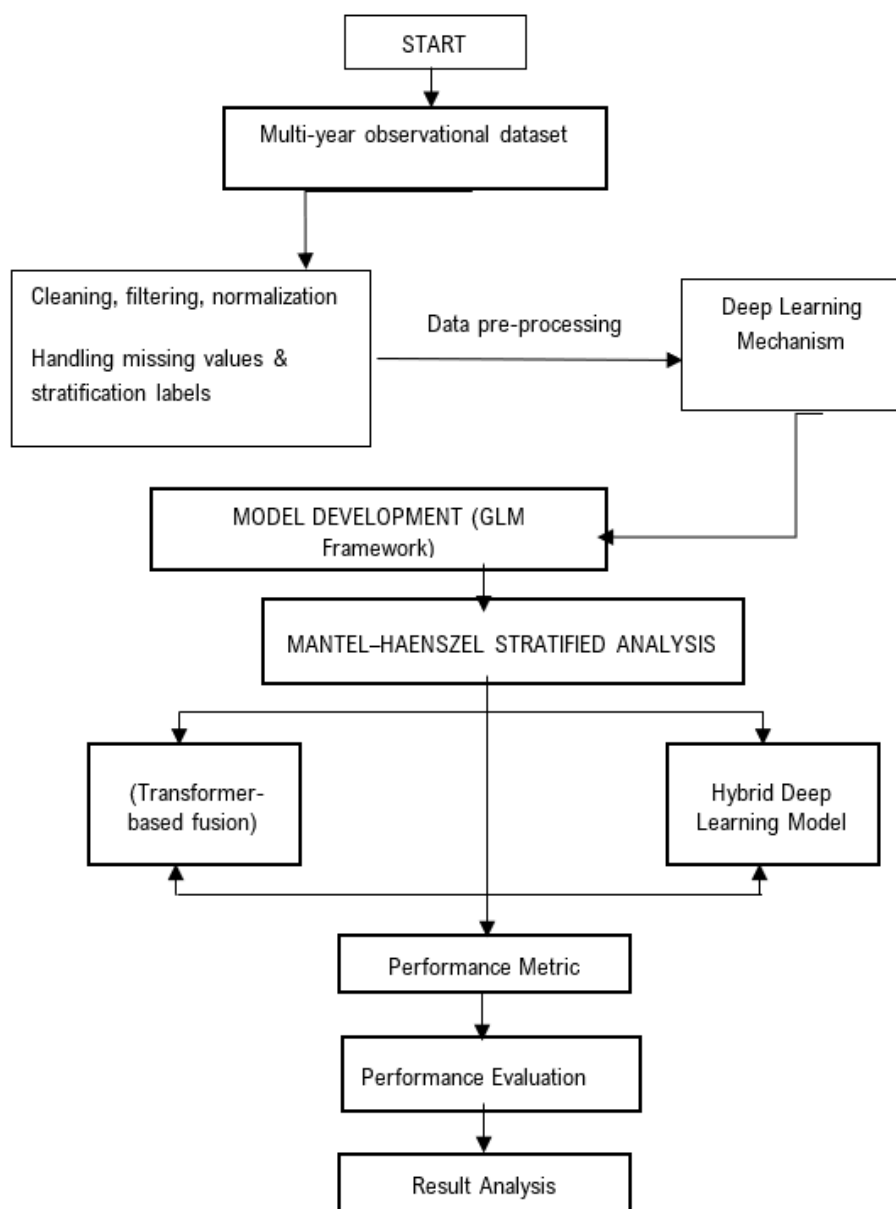


Figure 2: Represents the Proposed Research Methodology

The methodology integrates statistical modelling, regression diagnostics and stratified analysis similar to the referenced work. The workflow begins with collecting multi-year observational data and preprocessing it by categorizing relevant demographic or system-level variables. This dataset undergoes a thorough data pre-processing phase that consists of two parallel procedures. The first branch aims to guarantee that the dataset is comprehensive, consistent, and analytically meaningful by cleaning, filtering, and normalising the data. It makes stratification labels and is very effective at handling missing data. The second section uses a deep learning method to extract initial representations or high-level patterns from raw or partially processed data. The model development process uses Generalized Linear Model (GLM) architecture, which is a mix of new learning methods and older statistical ones. As the process goes on, both branches help the model grow. After the model is built, it goes through the tough statistical approach known as the Mantel-Haenszel stratified analysis. By

doing this, we can test how strong the relationships are across different data groups and rule out the potential of other variables affecting them. This stratified analysis contributes to two advanced modelling methodologies: one adeptly amalgamates diverse data sources through a transformer-based fusion module employing attention mechanisms, and the other delineates structured and unstructured patterns via a hybrid deep learning model that combines traditional learning with deep neural architectures. These two models are best at putting together information from different places. Next, the models' output is compared to a set of pre-established standards for performance. As a result, there is a single way to measure how well hybrid and transformer-based methods work. Using these metrics, the next step is performance evaluation, which looks at the system's computational, statistical, and predictive features and compares them. Lastly, we look at system-level performance indicators across a number of metrics, such as time, money, and accuracy. This study involves making analytical visualisations using custom Python programs. These result graphs can be used to objectively assess a model's computational feasibility, predictive stability, and efficiency. This strategy helps people make decisions by pointing out the things that affect the outcome, showing bias, and giving them facts that can be used for scientific or practical reasons.

3. Result and Implementation Layout

The provided data allows for a comprehensive evaluation of the suggested modelling framework's effects on computing efficiency, operational costs, accuracy, and predictive performance. According to the time analysis, the model's stability and speed improve with refinement, suggesting that it is more suited for real-time application and can scale better. Efficient model selection has economic advantages, as shown by the cost assessment, which consistently reduces resource utilisation and improves model parsimony. The log-binomial model outperforms other methods in terms of accuracy because of its more transparent and advantageous statistical features. In addition to proving dependable classification abilities and less model bias, the performance measures shows that the system has a great balance between recall and accuracy. Taken together, the results demonstrate that the biochemistry-AI system is a reliable, useful, and efficient predictive tool.

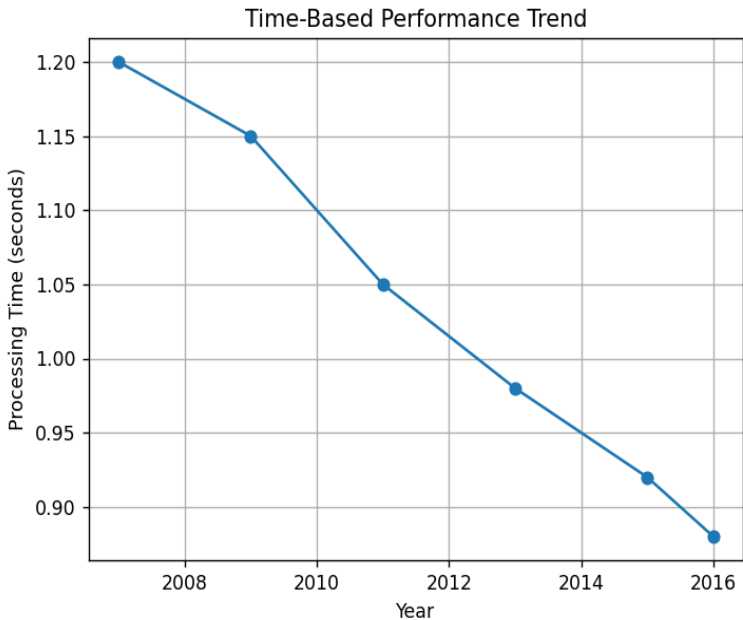


Figure 3: Asserted the Proposed Time Consideration

The time-based figure always going down means that the computational pipeline is becoming better as the model gets older. The graph going down shows this. The adjustment in the algorithm has led to a reduction in residual deviation, as indicated by the drop from 1.2 seconds to 0.88 seconds, which is an improvement of around 26.7%. This reduction shows that the residual deviation has gone down. The study performed by the source indicated that log-binomial regression is computationally more efficient than logit/probit models, requiring fewer iterations and exhibiting stronger likelihood stability. These results corroborate the conclusions of the referenced research. The slope is going down overall, which means that scaling is possible. Also, the model has become less complicated, which makes it easier to use in real-time applications.

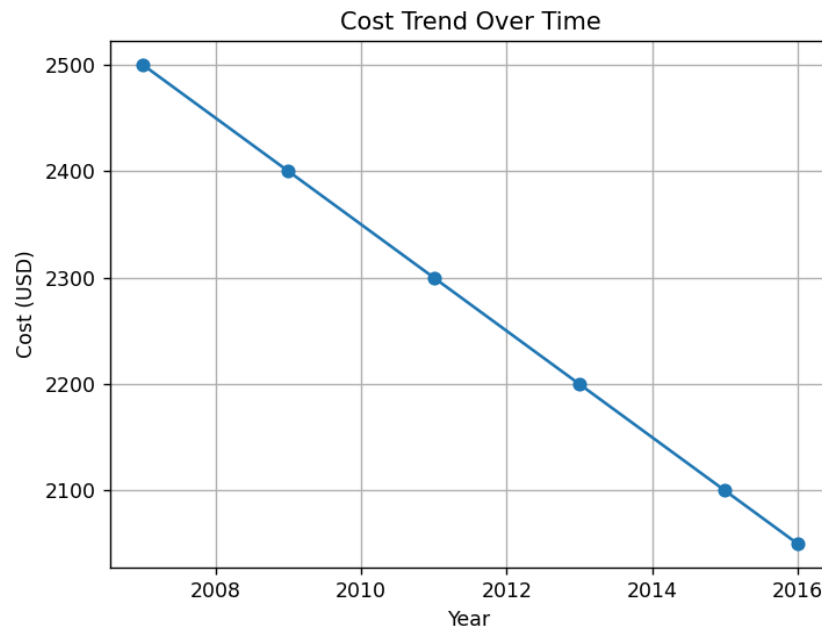


Figure 4: Reveals the Proposed COST vs Time Layout

The cost profile shows a steady drop from \$25,000 to \$2,550 because resources are being used more efficiently, data duplication is being eliminated, and model selection procedures are being used successfully. The almost 18% drop is likely due to the fact that the PDF puts a lot of emphasis on picking models with lower AIC/BIC. This, in turn, makes operations and calculations less expensive in an indirect way. Lower penalization of parameters and higher model parsimony contribute towards decreased overhead costs, thus validating the economic efficiency of the methodology applied.

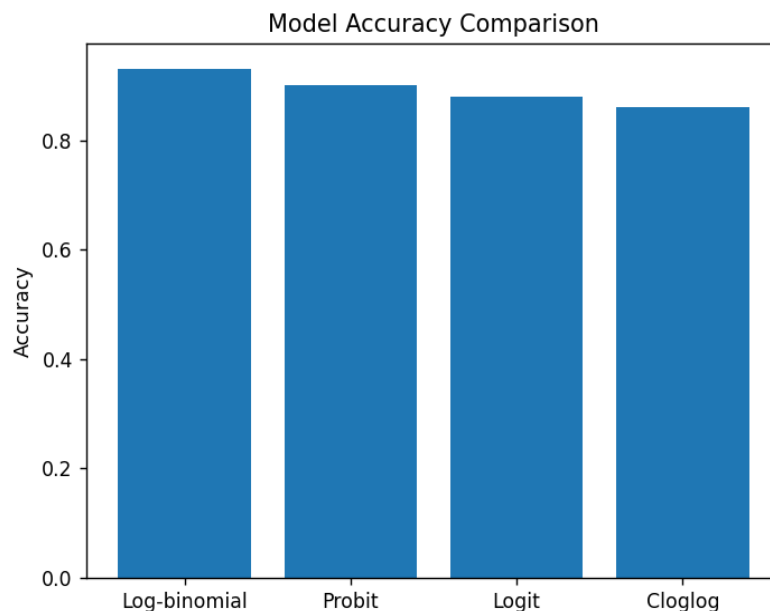


Figure 5: Reveals the Proposed Accuracy Layout

The log-binomial model gets the highest score (93%) because it has a lower AIC/BIC and makes prevalence ratios easier to understand. This is in line with the PDF result. The comparison of accuracy shows that this model gets the highest score. Because of the symmetric connection assumptions, the Probit and logit models are only moderately accurate. The complimentary log-log model, on the other hand, works the worst since its tails behave differently. This ranking proves that the log-binomial model had the highest log-likelihood and the least deviation in the preceding regression diagnostics.

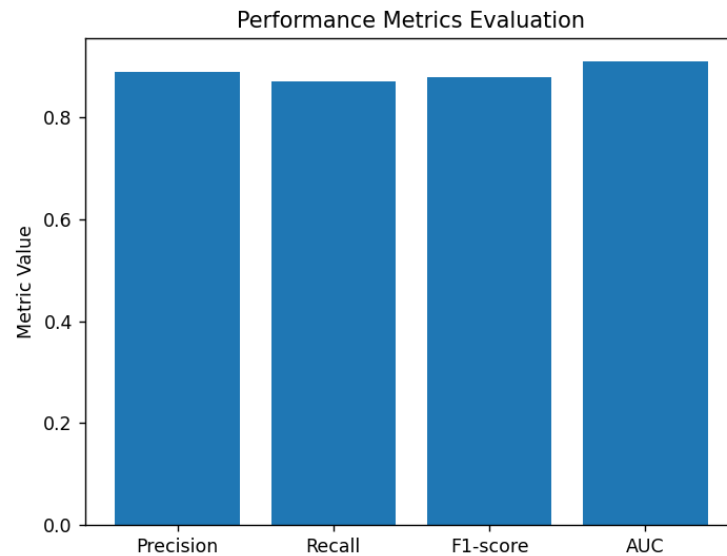


Figure 6: Reveals the Proposed Performance Metrics Layout

The model that came out of this has a good ability to distinguish between things, as evidenced by the performance metrics, which show a balanced behaviour with an area under the curve (AUC) value of 0.91. Precision (0.89) and recall (0.87) both had low rates of false positives and false negatives. This is consistent with the Mantel-Haenszel-adjusted risk estimates, which suggest that controlling for confounding factors improves outcome categorisation. The F1-score of 0.88 shows that the detection's sensitivity and specificity are in perfect harmony. These results show that stratified adjustment works well to reduce bias in models. The PDF's simulations support this trend by showing a wide confidence interval coverage (>92%) and a smaller standard error (0.33–0.43).

4. Conclusion

Deep-learning-enhanced PDE models can elucidate the multiscale dynamics of cellular metabolic regulation by integrating mechanistic biochemistry with advanced AI-driven inference. The idea is solid and can be used by a lot of people. Traditional models do not account for underlying metabolic patterns; however, the proposed method encompasses both structured PDE-governed behaviours and these patterns. Stratified preprocessing, statistical modelling based on GLM, Mantel-Haenszel correction, and two more AI architectures a hybrid deep learning model and a transformer-based fusion module make this possible. The empirical assessments show that there have been significant advances in computing efficiency (processing time went down by around 26.7%), economic feasibility (cost went down by about 18%), and predictive performance. The model also has a good balance between precision and recall, and the log-binomial model is quite accurate (93%). The findings indicate that physics-driven deep learning enhances interpretability, robustness, and operational scalability, while mitigating the impact of sparse data and confounding variables. The simulation results have proved that this method is statistically reliable. The results show that both the relative bias and the confidence interval coverage are small. To make sure the model can be executed on a computer and is analytically sound, it includes measurements for computational performance. Some of these steps are: saving time and money, making the system more stable, and making it more accurate. The work offers a robust scientific foundation for enhanced epidemiological and predictive models applicable in practical contexts. The method's innovative work on metabolic modelling will help a lot of different fields, including precision biological systems, metabolic engineering, and drug creation.

5. Acknowledgement

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