Pharmaformer: A Transformer-based pharmacokinetic prediction system

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Abstract. Traditional pharmacokinetic tools, such as NONMEM (Nonlinear Mixed Effects Modeling), have long been the standard for modeling drug concentration over time. However, these tools face significant limitations, including high costs, a steep learning curve, and reliance on outdated computational techniques, making them inaccessible to smaller medical institutions. To address these challenges, we propose Pharmaformer, a Transformer-based pharmacokinetic prediction system. Leveraging the advanced capabilities of Transformer models in capturing complex temporal patterns, Pharmaformer enables precise and interpretable predictions of drug concentrations. The system integrates data preprocessing, model inference, and results output into a user-friendly and cost-effective framework. Experimental results demonstrate that Pharmaformer outperforms the traditional FOCE algorithm, which follows the same principles as the one in NONMEM, in key metrics, offering a modern and accessible alternative for pharmacokinetic modeling. This system lowers barriers to entry while enhancing prediction accuracy, offering clinicians and researchers an innovative tool for improved pharmacokinetic analysis.

Keywords: Pharmacokinetics · Transformer · Prediction System.

1 Introduction

Predicting drug concentration in human blood over time is crucial for clinicians in determining optimal dosage regimens. This process, known as pharmacokinetics, provides a deep understanding of drug absorption, distribution, metabolism, and excretion, thereby helping doctors select the appropriate dosage and timing. Currently, tools like NONMEM[4] are widely used in hospitals for constructing

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[4] https://www.iconplc.com/solutions/technologies/nonmem

drug metabolism models. However, NONMEM requires a paid license and significant expertise in mathematics and statistics, making it difficult for smaller medical institutions with limited resources to use this tool.

Although NONMEM has been successful as a classic tool in drug metabolism research, its algorithms are relatively outdated and do not take full advantage of recent advances in computational methods. Additionally, the high cost and steep learning curve of NONMEM pose significant barriers to its broader adoption.

Pharmaformer addresses these challenges by integrating advanced Transformer-based deep learning techniques [1] into a free, easy-to-use pharmacokinetic prediction system. By automating complex steps and providing a user-friendly interface, Pharmaformer makes these advanced methods accessible to clinicians and researchers without requiring extensive expertise. This paper demonstrates the potential of modern deep learning techniques in drug metabolism modeling and provides a feasible tool for broader clinical use, aiming to lower the barrier to entry and improve prediction accuracy.

2 System Architecture and Key Techniques

In this section, we provide an overview of the Pharmaformer system, describe the architecture and key techniques, and compare the performance of our model with the FOCE [2] algorithm.

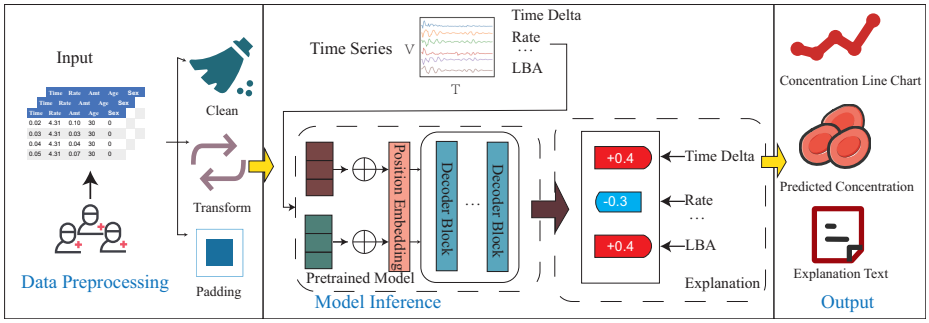


Fig. 1: System Workflow

2.1 Overview of the System

Figure 1 illustrates the Pharmaformer system's overall workflow, including data preprocessing, Transformer model inference, and results output. The figure provides an intuitive depiction of the entire data flow and processing steps, from raw input data to final predictions and explanation texts.

2.2 Model Architecture and Techniques

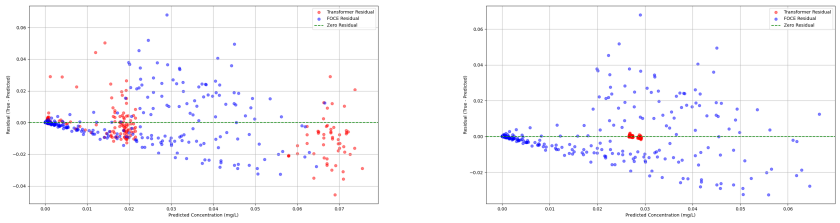
Our core model is a Transformer-based neural network specifically designed for time-series predictions. The architecture includes:

1. *Feature Extraction*: Extracts key features from input variables such as time, dosage, demographic information, and physiological parameters.
2. *Transformer Encoder*: Processes the sequential data to capture temporal dependencies.
3. *Output Decoder*: Predicts drug concentration for the next time step, using a regression-based output layer.

The model is optimized with a custom loss function to ensure accuracy in pharmacokinetic predictions. The data used for training and testing is sourced from a publicly available pharmacokinetics dataset[5].

Table 1: Comparison of Performance Metrics between Pharmaformer and FOCE, where ↑ indicates higher values for better performance and ↓ indicates lower values for better performance.

Methods	**MSE** ↓	**MAE** ↓	**RMSE** ↓	$\mathbf{R^2}$ ↑	**MAPE** ↓
Our model	0.000146	0.007148	0.012095	0.716216	87.45%
FOCE	0.000223	0.009869	0.014932	0.584882	92.96%



(a) (b)

Fig. 2: Residual Plots Comparing Pharmaformer (Without and With Normalization) with FOCE.

To evaluate our model, we compared it with the FOCE algorithm, which we implemented based on the same principles as the one in NONMEM. All performance evaluations were conducted by averaging the results after running 20 epochs. The FOCE algorithm uses unnormalized data because it requires physically meaningful units to estimate parameters such as clearance and volume of distribution—any rescaling would break the parametric assumptions imposed on the raw measurements. In contrast, our Transformer model, Pharmaformer, benefits significantly from data normalization and can utilize both unnormalized and normalized data (with normalization implemented in the preprocessing module). As detailed in Table 1, our model outperforms FOCE in all metrics. Figure 2 compares the residuals of our model and FOCE for predicted drug concentrations versus true values; note that a wide spread of points away from the zero residual line indicates poorer performance. In Figures 2 (a) and (b), our method shows a slight and absolute advantage, respectively, with normalized data further enhancing performance in Figure 2 (b).

[5] `https://www.kaggle.com/datasets/andrewsas26/pharmacokinetics-of-remifentanil`

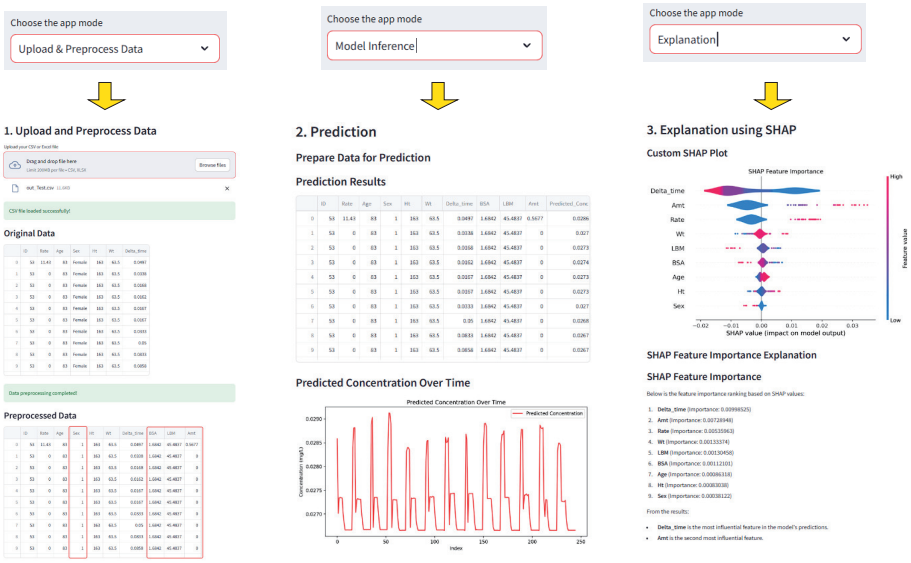


Fig. 3: Pharmaformer System GUI: Data Upload & Preprocessing, Model inference, Explanation

3 Demonstration

The demonstration video of Pharmaformer can be found at[6]. Figure 3 illustrates its user interface for data upload, preprocessing, model inference, and SHAP-based feature importance analysis. The system is intended as a clinical decision support tool rather than a fully autonomous solution; clinical validation is essential to address potential biases arising from incomplete or unrepresentative training data.

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References

1. Vaswani, A., Shazeer, N., Parmar, N., Uszkoreit, J., Jones, L., Gomez, A.N., Kaiser, Ł., Polosukhin, I.: Attention is all you need. In: Proceedings of the 31st International Conference on Neural Information Processing Systems (NIPS'17), pp. 6000–6010. Curran Associates Inc., Red Hook, NY, USA (2017).
2. Wang, Y.: Derivation of various NONMEM estimation methods. In: Journal of Pharmacokinetics and Pharmacodynamics, vol. 34, no. 5, pp. 575–593 (2007). DOI: 10.1007/s10928-007-9060-6.

[6] `https://github.com/Aalizz/Pharmaformer`