Pharmacokinetics-Informed Neural Network for Predicting Opioid Administration Moments with Wearable Sensors

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Motivation & Objectives

In light of the opioid epidemic's devastating impact on public health, there is an urgent need for innovative solutions to address opioid misuse and addiction. By leveraging wearable sensor technology to remotely monitor opioid administration and detect potential risks of opioid use disorder, our research aims to mitigate the adverse effects of this epidemic and improve patient outcomes. In this work, we:

1. Detect oral opioid administrations using physiological data from wristwatch.
2. Combine the pharmacokinetic information of opioids with wearable data, model-agnostically, to improve performance.

Materials & Methods

Pharmacokinetics (PK) studies drug processing in the body, including absorption, metabolism, distribution, and elimination, with a focus on tracking drug concentration changes in blood plasma over time. Opioids in our study adhere to first-order equations for drug plasma concentration, as defined by...

$$D_t \propto \underbrace{\boxed{D_0}}_{\text{drug amount administered}} \times \left(e^{-K_e \overbrace{\boxed{t}}^{\text{time since administration}}} - e^{-K_a t}\right) \qquad (1)$$

As the time of administration and type of opioid are known from EHR, we approximate the above equation and use it as an auxiliary loss along with opioid detection loss while training the model

$$Loss = \lambda_1 \underbrace{\boxed{L_{WCE}}}_{\text{Opioid detection loss}} + \lambda_2 \overbrace{\boxed{L_{KAPPA}}}^{\text{Moment prediction loss}} + \lambda_3 \overbrace{\boxed{L_{RMSE}}}^{\text{Auxiliary loss}} \qquad (2)$$

Introduction

Long-term use of opioids, intended for pain management, can result in an individual developing dependence on the drug, ultimately leading to Opioid Use Disorder (OUD) and potentially life-threatening risks. Utilizing multimodal data from wristwatch sensors, we remotely monitor opioid administrations, enabling healthcare professionals to intervene before individuals develop OUD. By employing models pretrained using self-supervised learning (SSL) methods, we initially detect opioid administration. Furthermore, **combining pharmacokinetic information of opioids with wearable data** during this training enables the model to detect moments of opioid administration with significantly improved performance.

Results 2

Poorer performance in opioid moment prediction motivated us to approximate Equation 1 and use drug plasma concentration level as an auxiliary task during the prediction.

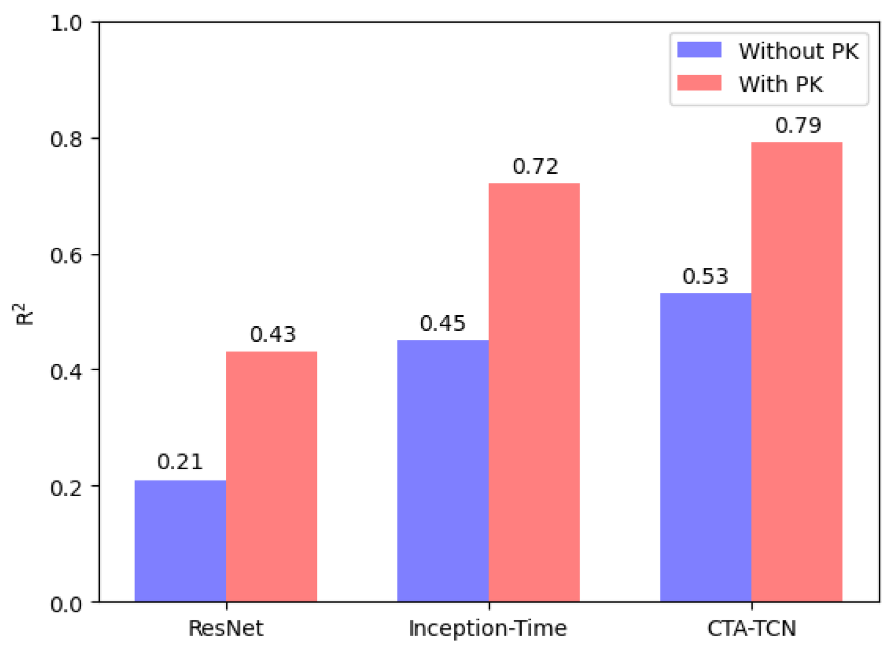

Figure 3: Using PK information improved the performance of opioid moment prediction across all the models

Results 1

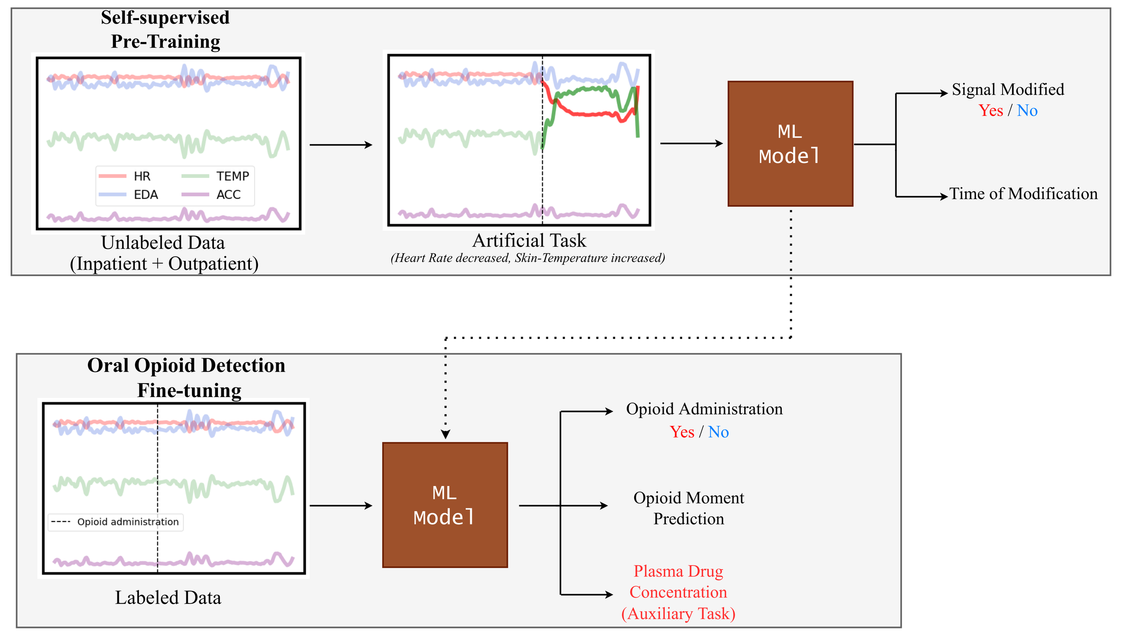

Figure 1: Pharmacokinetics-informed approach for monitoring opioid administrations combined with SSL

We develop a model that can take a timeseries window as input and generate two types of output: (i) binary opioid administration/use detection inference (i.e., if the opioid was administered in the input time-window); and (ii) predict the exact moment of Opioid administration/use in the time-window.

We train the model in two steps. In the first step, we use Self-supervised learning to teach the model how to detect sudden changes in different modalities in the wearable sensor data with a "pretext" task. We finetune this model to the opioid administration task.

Table 1: Binary Detection F1-score performance

Model	Without SSL	With SSL
ResNet	0.67	0.76
Inception-Time	0.70	0.75
CTA-TCN	0.73	0.79

Model	Without SSL	With SSL
ResNet	0.17	0.21
Inception-Time	0.33	0.45
CTA-TCN	0.49	0.53

Table 2: Opioid Moment prediction with R^2 performance

Conclusion

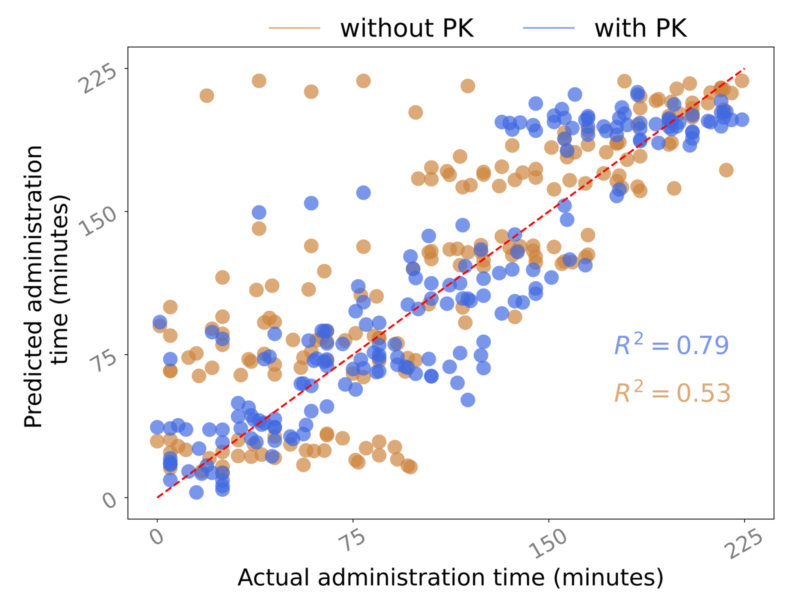

Figure 2: Scatter-plot highlighting the difference in predictions using PK-informed model

- Machine learning models trained on extensive wearable data successfully detect both the occurrence and timing of oral opioid administrations
- Integration of self-supervised learning modestly improves model performance, while the inclusion of opioid pharmacokinetic data significantly enhances the accuracy of predicting opioid use timing.

References

[1] Milo Gibaldi, Donald Perrier, et al. *Pharmacokinetics*, volume 15. M. Dekker New York, 1982.

[2] Gullapalli Bhanu, Tauhidur Rahman, et al. Opitrack. 2021.

Future Research

Current study uses oxycodone opioid that follows first order elimination and absorption. We plan to extend to other heterogeneous opioids that follow different order equations (ex:- Fentanyl)

Wearable data from the Empatica E4 and ground truth labels from EHR are utilized in this study. In cases of unreliable labels and noisy data, further model validation is necessary.

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