DOCTORAL THESIS

Deep Learning Models for Irregular Electronic Health Record Data Analysis

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Abstract

The wide adoption of electronic health records (EHR) produces a large quantity and variety types of health data, such as laboratory parameters, disease diagnoses, treatment reports, medication orders, as well as some basic health data (e.g., birth date, gender), which provides unprecedented opportunities for developing advanced machine learning models to detect high-risk patients, evaluate early treatment effects, and assist doctors to design more effective treatment plans, effectively improving healthcare quality and clinical outcomes.

However, the analysis of EHR data is challenging because real-world medical data is highly irregular (significantly varying time intervals between successive visits and severe missing data problem in the examinations of physiological variables) and heterogeneous (from stable basic health data to significantly changing laboratory parameters). First, influenced by the dynamic changes in the severity of illness, patients usually go to hospitals and take examinations irregularly, producing a large volume of irregular medical time-series data with varying intervals. Meanwhile, certain physiological variables are not examined during some visits to the hospitals, causing the missing data problem. Furthermore, there could be some relationships between different types of medical data, e.g., basic health data may influence future trajectories of dynamic variables. To handle these issues, in this thesis, a series of novel deep learning-based approaches are proposed for EHR data analysis.

In this thesis, we develop an uncertainty-aware neural network to deal with the irregular visit intervals. Existing methods often handle this problem by generating regular time series from the irregular medical records without considering the

uncertainty in the generated data, induced by the varying intervals. Thus, a novel Uncertainty-Aware Convolutional Recurrent Neural Network (UA-CRNN) is proposed in this thesis, which introduces the uncertainty information in the generated data to boost the risk prediction. To tackle the complex medical time series with sub-series of different frequencies, the uncertainty information is further incorporated into the sub-series level rather than the whole sequence to seamlessly adjust different time intervals. Specifically, a hierarchical uncertainty-aware decomposition layer (UADL) is designed to adaptively decompose time series into different sub-series and assign them proper weights in accordance with their reliabilities. Meanwhile, an Explainable Uncertainty-Aware Convolutional Recurrent Neural Network (eUA-CRNN) is proposed to exploit filters with different passbands to ensure the unity of components in each sub-series and the diversity of components in different sub-series. Furthermore, eUA-CRNN incorporates with an uncertainty-aware attention module to learn attention weights from the uncertainty information, providing explainable prediction results. Extensive experimental results on three real-world medical datasets illustrate the superiority of the proposed method compared with the state-of-the-art methods.

On the other hand, varying time intervals and missing values may provide valuable information in improving clinical prediction performance because visit intervals are usually determined by the health status of patients while missing values are caused by changes in symptoms of patients. As a result, the traditional strategy of processing irregular EHR data into regular data to fit the properties of standard machine learning models may damage the meaningful medical considerations in the irregular examination arrangements. Therefore, we develop a novel end-to-end Dual-Attention Time-Aware Gated Recurrent Unit (DATA-GRU) for irregular EHR data analysis to avoid damaging the informative varying intervals and missing data phenomenon. In particular, DATA-GRU is able to: 1) preserve the informative varying intervals by introducing a time-aware structure to directly adjust the influence of the previous status in coordination with the elapsed time, and 2) tackle missing values by proposing a novel dual-attention structure to jointly consider data-quality and medical-knowledge. A novel unreliability-aware attention mechanism is designed to handle the diversity in the reliability of different data, while a new symptom-aware attention mechanism is proposed to extract medical reasons from original clinical records. Extensive experimental results on two real-world datasets demonstrate that DATA-GRU can significantly outperform the state-of-the-art methods and provide meaningful clinical interpretations.

Furthermore, since multiple data sources (e.g. dynamic laboratory parameters, static basic health data) can reflect different aspects of the health conditions of patients, designing a framework to effectively combine them for clinical predictions will potentially improve the performances. To this end, in this thesis, we develop a novel End-to-end Importance-Aware Personalized Deep Learning Approach (eiPDLA) to achieve accurate early clinical risk prediction. Specifically, eiPDLA introduces a Long Short-Term Memory with Temporal Attention to learn sequential dependencies from time-stamped records and simultaneously incorporating a Residual Network with Correlation Attention to capture their influencing relationship with static medical data. Furthermore, a new Multi-Residual Multi-Scale Network with the importance-aware mechanism is designed to adaptively fuse the learned multi-source features, automatically assigning larger weights to important features while weakening the influence of less important features. Extensive experimental results under various settings on real-world medical data illustrate that the proposed method significantly outperforms the state-of-the-art methods. Case studies indicate that the achieved prediction results are highly interpretable.

The main contributions of this thesis are summarized as follows.

- We propose a novel explainable uncertainty-aware neural network to incorporate the uncertainty information in the generated data to dynamically learn contribution weights of different data and introduce filters to adaptively adjust the unity of components in each sub-series and the diversity of components between different sub-series. Meanwhile, an attention module is incorporated to identify key features and provide explainable prediction results.

- We propose a novel dual-attention time-aware neural network to jointly deal with the two key challenges (i.e., varying time intervals and missing values) in irregular EHR data by preserving the contained useful information on dynamic changes in the health status of patients.
- We propose a novel end-to-end importance-aware approach to simultaneously model multiple data sources, including both static and dynamic health data, while adaptively learning fusion weights for different deep features and assign larger weights to important features.

Keywords: irregular EHR data analysis, uncertainty-aware prediction, dual-attention mechanism, explainable prediction results, multiple data sources

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