MedFACT: Modeling Medical Feature Correlations in Patient Health Representation Learning via Feature Clustering

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Abstract

In healthcare prediction tasks, it’s essential to exploit the correlations between medical features and learn better patient health representations. Existing methods try to estimate feature correlations only from data, or increase the quality of estimation by introducing task-specific medical knowledge. However, such methods either are difficult to estimate the feature correlations due to insufficient training samples, or cannot be generalized to other tasks due to reliance on specific knowledge. There are medical researches revealing that not all the medical features are strongly correlated. Thus, to address the issues, we expect to group up strongly correlated features and learn feature correlations in a group-wise manner to reduce the learning complexity without losing generality. In this paper, we propose a general patient health representation learning framework MedFACT. We estimate correlations via measuring similarity between temporal patterns of medical features with kernel methods, and cluster features with strong correlations into groups. The feature group is further formulated as a correlation graph, and we employ graph convolutional networks to conduct group-wise feature interactions for better representation learning. Experiments on two real-world datasets demonstrate the superiority of MedFACT. The discovered medical findings are also confirmed by literature, providing valuable medical insights and explanations.

1 Introduction

Nowadays, as electronic medical systems are ubiquitously deployed in hospitals and healthcare centers worldwide, massive electronic health records (EHR) have been rapidly collected. EHR is a kind of multivariate time series data, which records various medical features of patients, mainly including static features (e.g., age, gender) and dynamic features (e.g., diagnoses, lab test results). Recently, deep learning methods have been applied to various health prediction tasks, such as mortality predictions [Ma et al., 2020], diagnosis predictions [Ma et al., 2018], etc. In those tasks, deep learning methods extract patient health representations from massive EHR data, which both effectively and intelligently help doctors estimate patient health status, and conduct targeted treatments to prevent adverse outcomes.

In EHR data, there often exist underlying correlations between medical features. For instance, [Kamal, 2014] discovers the phenomenon that the simultaneous increase of urea and creatinine can indicate kidney dysfunction, which reveals the strong correlations between those features for patients with chronic kidney disease. Therefore, it’s of great significance to exploit the inherent correlations between medical features and learn a better patient health representation for downstream prediction tasks.

Some existing works try to learn feature correlations with sophisticated deep learning architectures directly from EHR data [Choi et al., 2016; Song et al., 2018; Ma et al., 2020]. Those networks are designed with highly-parameterized dense layers to deal with high-dimensional medical features and formulate enormous hypothesis spaces. However, there are often abundant medical features but limited patient samples in EHR data [Zhang et al., 2019]. Therefore, it’s diffi-
cult for deep models to directly learn the correlations between massive features from insufficient patient samples. Some other works attempt to mitigate this problem by incorporating external prior medical knowledge in deep models [Choi et al., 2017; Ma et al., 2018; Lu et al., 2021]. Those methods utilize various kinds of medical knowledge (e.g., hierarchy of disease code, medical literature) as priors to constrain the hypothesis space of deep networks, which can reduce learning complexity with instructions from prior knowledge. However, those methods are strongly dependent on precise task-specific knowledge, which is time-consuming and hard to obtain and lack of generalization. Besides, those methods are not suitable for patient cohorts who suffer from rare diseases or emerging epidemics (e.g., COVID-19), for human experts are lack of knowledge and experience for those diseases.

To tackle the shortcomings above, we expect an approach to constrain learning complexity in deep models while ensuring strong generalization ability at the same time. Medical researches have revealed that the medical features are not always correlated in the same way. Here is a motivating example. [Harbath et al., 2001] proposes that for sepsis patients, several indicators of cytokines level (e.g., PCT, TNF-α) are strongly correlated, while correlations between cytokines and inflammation indicators (e.g., hs-CRP) are weak. Therefore, as illustrated in Figure 1, we can conclude a prior assumption that medical features can be divided into groups by their correlations, where features in the same group are strongly correlated, and features from different groups are not or weakly correlated. Then, we can intuitively simplify correlation estimation of all features into several group-wise correlation estimations to reduce the dimension of features in each group and constrain the learning complexity.

Formally, we denote medical features as multi-dimensional stochastic variables $z_i$ (i.e. $i$-th medical feature), and our objective, feature correlation learning, is equivalent to approximating the joint probability distribution of features $p(Z) = p(z_1, z_2, \ldots, z_F)$. We group up features with strong correlations and formulate $K$ subsets of features $\{G_1 | G_2 | \cdots | G_K\}$, and consider latent features $L$ depicting the weak correlations between groups, whose dimension is far less than $Z$. We present our prior assumption mathematically:

**Assumption 1** Given latent features $L$, features from different groups are conditionally independent:

$$p(Z) = p(G_1, G_2, \cdots, G_K) = p(G_1 | L)p(G_2 | L)\cdots p(G_K | L)p(L) \tag{1}$$

This provides a solution to simplify the approximation of joint distribution $p(Z)$, which is reducing $p(Z)$ to several sub-problems that approximate group-wise feature distributions $p(G_i | L)$ and latent inter-group feature distribution $p(L)$ with much less features and lower learning complexity.

However, there remain two practical challenges to realize Assumption 1:

1. **What is the metric space to measure the correlation between medical features?** It’s necessary to measure feature correlations to divide features into groups reasonably. For better generalization, we try to measure correlations from data without task-specific external priors. However, this is still a challenging problem of two entangled perspectives. 1) What is the space to measure? The noise-to-signal ratio is too high in the original representation space, and the coordinate of different features is not well aligned. A feature mapping guided by the supervised signal could possibly fix this issue. 2) Which metric to use? The support of samples in the latent representation space is a non-Euclidean manifold. This makes it hard to calculate the similarities between samples as well as the correlations between features.

2. **How to learn group-wise and inter-group feature distributions $p(G_i | L)$ and $p(L)$?** It seems straightforward to mask off the feature correlations from different groups to learn group-wise distributions $p(G_i | L)$, such as masked self-attention mechanism. However, those methods cut off all feature interactions between groups, which cannot solve the latent feature distributions $p(L)$. Therefore, it’s worth thinking about how to learn $p(G_i | L)$ and $p(L)$ at the same time.

To address the challenges above, in this paper, we propose a general patient health representation learning framework MedFACT (Medical FeAture ClusTering). Our main contributions are summarized as follows:

- We propose a general health representation learning framework MedFACT to reduce the learning complexity while capturing correlations between medical features, which does not rely on any task-specific external priors.
- Specifically, addressing challenge 1, MedFACT designs a way to group up features according to their underlying correlations exploited from data. We measure feature correlations by computing cohort-wise similarities between temporal patterns of features learned under supervision through a characteristic kernel. The kernel is capable of capturing long-term and short-term dependencies in the signal [Gretton et al., 2012]. Then we apply spectral clustering algorithm to group up features according to the correlations.
- Addressing challenge 2, we formulate the feature group structure as a correlation graph, and graph convolutional network is employed to learn group-wise and latent inter-group feature distributions simultaneously.
- Extensive experiments on two real-world datasets demonstrate that MedFACT significantly outperforms the state-of-the-art methods under various settings. Besides, the discovered findings are confirmed by medical literature, and can also provide valuable medical insights and explanations.

2 **Related Works**

There are various works trying to learn feature correlations to generate better health representations for downstream prediction tasks. Some existing works attempt to learn feature correlations directly from data. For example, RETAIN [Choi et al., 2016] employs two RNNs to learn different attention weights for visits and medical features. TimeNet [Gupta et al., 2018] designs a shared RNN to learn different features respectively and learn correlations via a linear layer. TimeLine [Bai et al., 2018] and ConCare [Ma et al., 2020] both apply self-attention mechanism to learn feature correlations. Some other works try to learn feature correlations more accurately by incorporating task-specific medical knowledge. GRAM [Choi et al., 2017] and KAME [Ma et al., 2018] both
incorporate hierarchy of disease codes to enhance learning. CGL [Lu \textit{et al.}, 2021] combines patient personal information with domain knowledge to construct a graph, and uses GCNs to learn better representations. However, as discussed before, all the methods above are either difficult to learn feature correlations due to insufficient training samples, or lack of generalization due to reliance on task-specific knowledge. While our method, \textsc{MedFACT}, can better estimate feature correlations via reducing hypothesis space and learning complexity. Meanwhile, \textsc{MedFACT} does not rely on any task-specific knowledge, which has better generalization ability.

3 Problem Formulation

Electronic Health Records (EHR) data consist of dynamic and static information of patients. For every patient, assuming that there are $F$ dynamic medical features (e.g., lab tests, vital signs) recorded at every clinical visit $t$, the visit can be recorded as a vector $x_t \in \mathbb{R}^F$. Supposed that there are $T$ visits, the dynamic information can be formulated as a 2-dimensional matrix $X = [x_1, x_2, ..., x_T]^\top \in \mathbb{R}^{T \times F}$. The static information (e.g., demographics) is recorded only once during the whole visits, and can be formulated as a vector $s \in \mathbb{R}^S$, where $S$ denotes the number of static features.

In this paper, our predictive objective can be presented as a clinical outcome prediction task. Given the EHR of a patient as inputs, our algorithm attempts to predict the probability of suffering a specific clinical outcome (e.g., mortality), denoted as $y \in \{0, 1\}$. We pose this task as a binary classification problem, namely, $\hat{y} = \textsc{MedFACT}(X, s)$.

4 Methodology

Figure 2 illustrates the general framework of \textsc{MedFACT}, which comprises the following modules:

- **Feature Embedding Module** learns representations individually for every dynamic and static features.
- **Feature Clustering Module** estimates feature correlations with obtained representations, and the features are clustered into groups according to the estimated correlations.
- **Feature Correlation Graph Construction Module** constructs an edge-weighted correlation graph based on the feature groups and their correlations.
- **Graph-based Feature Interaction Module** employs GCN to learn group-wise and latent inter-group feature distributions based on the correlation graph.
- **Prediction Module** applies attention mechanism and linear layers to generate a comprehensive health representation and conduct specific prediction tasks.

4.1 Feature Embedding

In \textsc{MedFACT}, we expect to estimate the correlations between medical features, which are indicated by similar developing patterns along visits (i.e., simultaneous rising/descending). Therefore, \textsc{MedFACT} attempts to learn representations and extract temporal patterns for every feature from their sequential visits separately. To address our issue, we utilize multi-channel Gated Recurrent Units (GRU) to extract temporal patterns for every feature individually. Specifically, we employ $F$ different GRUs for $F$ features. Each feature $x_i$ can be formulated as a time series (i.e., $x_i = [x_{i1}, x_{i2}, ..., x_{iT}]$), and will be fed into the corresponding GRU for embedding:

$$h_{iT} = \text{GRU}_i(x_{i1}, x_{i2}, ..., x_{iT}), i = 1, 2, ..., F$$

The static features are also embedded into the hidden space with a linear layer: $h_s = s \cdot W_s$. Now that we have obtained representations of all features, yet their representation spaces remain unaligned. Therefore, we map all the embeddings into an aligned representation space via a shared activated linear projection $W_{proj}$:

$$z_i = \text{ReLU}(h_{iT} \cdot W_{proj}), i = 1, 2, ..., F$$

$$z_s = \text{ReLU}(h_s \cdot W_{proj})$$

And the representation matrix $Z$ stands for the stacked representations: $Z = [z_1, z_2, ..., z_F, z_s]^\top$.

4.2 Feature Clustering

**Feature Correlation Estimation**

In \textsc{MedFACT}, we expect to divide features into groups according to their correlations in order to simplify the approximation of $p(Z)$. Thus, it’s necessary to estimate correlations between features from a cohort-wise perspective. We suggest that the correlations between two features can be implied by similar temporal patterns that widely appear in the patient cohort. Now that the temporal patterns of each feature $i$ are extracted by the GRU embedded feature representation $z_i$ under the supervision of labels, it’s natural to consider the cohort-wise similarities of $z_i$ as the feature correlations.

In \textsc{MedFACT}, we employ the characteristic kernel method [Gretton \textit{et al.}, 2012] to measure the sample-wise similarity of two features in non-Euclidean latent space. Here we select Laplacian kernel (i.e. $k(x, y) = \exp(-\|x - y\|_2)$) as the kernel function. We suppose that the cohort-wise similarities can be approximated by the average of sample-wise similarities, and the correlations between two features $i$ and $j$ can be defined as:

$$r_{ij} = \frac{1}{N} \sum_{n=1}^{N} k(z_i^{(n)} \cdot z_j^{(n)}).$$

Thus the correlations between all features can be formulated as a matrix $R = (r_{ij})_{F \times F}$.

**Correlation-based Feature Clustering**

\textsc{MedFACT} attempts to apply clustering algorithms to group up features based on the learned correlations, and expects to make features in the same group have stronger correlations. In detail, \textsc{MedFACT} utilizes K-Means based spectral clustering algorithm [Stella and Shi, 2003] to cluster all $F$ dynamic features into $K$ groups based on the pre-computed affinity matrix $R$. We denote the $K$ groups as subsets of features (i.e., $G_1, G_2, ..., G_K$), satisfying:

$$\bigcup_i G_i = \{z_1, z_2, ..., z_F\}; \quad G_i \cap G_j = \emptyset, \forall i \neq j$$

The optimization objective of spectral clustering can be formulated as follows:

$$\min_{G_1, G_2, ..., G_K} \sum_{i=1}^{K} \sum_{z_i \in G_k} \sum_{z_j \notin G_k} r_{ij},$$

where $r_{ij}$ is the correlation between features $i$ and $j$. This optimization problem can be solved by the spectral clustering algorithm [Nips, 2003], which can guarantee the optimal solution when the number of groups $K$ is pre-specified.
which aims to minimize the sum of correlations between the features from different groups. Besides, we also assume that all the dynamic features are strongly related with static features, and we make static features belong to every group:

$$G_i := G_i \cup \{z_s\}, \ i = 1, ..., K$$  

(7)

4.3 Feature Correlation Graph Construction

We try to model the group structure of medical features in a more plain view. Intuitively, we convert the feature group structure to a specific correlation graph, where the graph nodes denote medical features, and their connections denote the group-wise correlations. Concretely, there are \(F+1\) nodes in the graph, including \(F\) dynamic feature nodes and one static feature node. The weighted edge between nodes denotes the correlations between features. We use an adjacency matrix \(A\) to represent the graph, whose element \(a_{ij} \in [0,1]\) denotes the correlation weight between feature \(i\) and \(j\). There are three specific graph construction rules:

- All the dynamic features from the same feature group \(k\) are connected with each other, forming a fully connected sub-graph. Specifically, for any dynamic feature pair \(z_i, z_j \in G_k, i \neq j\), there’s an edge between them, and \(a_{ij} = 1\).

- For the static feature node, we have supposed that all the features are strongly related with it. Specifically, there’s an edge between every dynamic feature \(z_i\) and the static feature, and we set the correlation weight \(a_{i(F+1)} = 1\).

- All the features are self-related, which means there’s a self-connection on every feature \(z_i\), weighted \(a_{ii} = 1\).

The topology of the constructed feature correlation graph is illustrated in Figure 2, where different colors of feature nodes denote different groups, and edges denote the correlations.

4.4 Graph-based Feature Interaction

According to Assumption 1, approximation of \(p(Z)\) is reduced to sub-problems solving group-wise feature distributions \(p(G_i|L)\) and latent inter-group feature distribution \(p(L)\). Inspired by Graph Convolutional Network (GCN) [Kipf and Welling, 2016], MedFACT tries to interact information from neighbor nodes based on the correlation graph, and apply 2 GCN layers to solve \(p(G_i|L)\) and \(p(L)\) respectively.

Specifically, a GCN layer \(g_l(\cdot)\) conducts feature transformation with a parameter matrix \(W_l\) and further interacts features from all neighbor nodes based on adjacency matrix \(A\):

$$g_l(Z) = \text{ReLU}(AZW_l),$$  

(8)

where the footnote \(l\) denotes the \(l\)-th layer of GCN. Due to the special property of the correlation graph, the first layer of GCN \(g_1(Z)\) only conducts interactions between feature nodes in the same group, which learns the group-wise conditional joint distributions \(p(G_i|L)\). After \(g_1(Z)\), the static feature node combines information from all features. Therefore, in the second layer of GCN \(g_2(Z)\), all the feature nodes can extract information from any other features via static node. That means besides group-wise correlations, \(g_2(Z)\) can also learn the latent feature distribution \(p(L)\) that depicts the weak inter-group correlations.

After two layers of GCN, we have solved all the reduced sub-problems and is able to approximate the joint distribution \(p(Z)\). The features after interaction are denoted as a matrix \(Z^* = [z_1^*, z_2^*, ..., z_F^*, z_s^*]^T\), where:

$$Z^* = g_2(g_1(Z)) = \text{ReLU}(A \text{ReLU}(AZW_1) W_2).$$  

(9)

4.5 Prediction Layers

Finally, a comprehensive health representation of a patient is expected to perform the personalized prediction. Here we introduce an attention mechanism to summarize information from the representations \(Z^*\). Concretely, we use the representation of static features \(z_s^*\) to obtain the query \(q_s\), while the keys \(k_i\) and values \(v_i\) are obtained by \(z_i^*\):

$$q_s = z_s^* \cdot W_q; \quad k_i = z_i^* \cdot W_k; \quad v_i = z_i^* \cdot W_v, \ i = 1, 2, ..., F, s$$  

where \(W_q, W_k, \text{ and } W_v\) are projection matrices, and the attention weights \(\alpha_i\) are calculated as:

$$\tau_i = \tanh(q_s^T k_i), \quad \alpha_1, ..., \alpha_F, \alpha_s = \text{Softmax}(\tau_1, ..., \tau_F, \tau_s).$$  

(11)
The comprehensive health representation $e$ is obtained by weighted sum of values $v_i$, and we use a linear layer to conduct the final prediction task based on $e$:

$$ e = \sum_{i=1}^{F} \alpha_i v_i + \alpha_s v_s, \quad \hat{y} = \text{Sigmoid}(e \cdot W_{\text{pred}}). \quad (12) $$

Finally, the cross-entropy loss is applied as the loss function:

$$ \mathcal{L} = -y \log(\hat{y}) - (1 - y) \log(1 - \hat{y}), \quad (13) $$

where $\hat{y} \in [0, 1]$ is the predicted probability and $y$ is the ground truth. We present the detailed algorithm of MedFACT in Algorithm 1. It’s worth mention that in order to ensure stability in training, we don’t always update the correlation graph at the end of every training epoch. After certain epochs (i.e., CLUSTER\_EPOCHS), the correlation graph is fixed and no longer updated. In experiments, we empirically set CLUSTER\_EPOCHS to 20% of the total training epochs.

### Algorithm 1 MedFACT ($X, s$)

1. **Initialization:** Set all elements in correlation matrix $R$ to 1. Randomly initiate $K$ clusters and construct the correlation graph following Section 4.3.
2. **while** $E$ in epochs **do**
3.   **for** $B$ in mini-batches **do**
4.     Compute batch loss function $\mathcal{L}$
5.     Update parameters of MedFACT by optimizing $\mathcal{L}$
6.   **end for**
7.   **if** $E < \text{CLUSTER\_EPOCHS}$ **then**
8.     **for** $i$ in $1,2,...,F$ **do**
9.       **for** $j$ in $1,2,...,F$ **do**
10.      Calculate $R[i,j] = 1 \over N \sum_{n=1}^{N} k(z_i^{(n)}, z_j^{(n)})$
11.     **end for**
12. **end for**
13. Cluster features to $K$ groups $\{G_i\}_{i=1}^{K}$ according to the correlations $R$, and update correlation graph $A$.
14. **end if**
15. **end while**

## 5 Experiments

### 5.1 Dataset Descriptions

**CKD Dataset** We conduct mortality prediction task on a real-world chronic kidney disease (i.e., CKD) dataset, including CKD patients who received therapy from January 1, 2006, to March 1, 2018, in a real-world hospital.\(^1\) The mortality prediction task is formulated as a binary classification task, predicting whether the patient dies unfortunately within a year after the last visit. The cleaned dataset consists of 662 patients with 17 dynamic features (e.g., glucose) and 4 static features (e.g., gender). The detailed statistics are presented in Appendix. Due to the scarcity of CKD data, 5-fold cross-validation experiments are performed.

**Cardiology Dataset** Another dataset we use is an open-source PhysioNet cardiology dataset [Reyna et al., 2019], which is collected from three geographically distinct U.S. hospitals over the past decade. The patients in the dataset are binary labeled by Sepsis-3 clinical criteria, and we conduct the sepsis prediction on it. This dataset is highly imbalanced, with only 7.26% of samples labeled positive. The cleaned dataset consists of 40,336 patients with 34 dynamic features and 5 static features, and the detailed statistics are presented in Appendix. The dataset is randomly divided into the training, validation, and testing set with a proportion of 8:1:1.

### 5.2 Experimental Setups

We implement our methods with PyTorch v1.7.1 and conduct experiments on a machine equipped with GPU: Nvidia Quadro RTX 8000. While training models, Adam optimizer is employed with learning rate set to 1e-3. To fairly compare different approaches, the hyperparameters of the models are fine-tuned by grid search on training sets. Specifically, for Cardiology dataset, the number of clusters $K$ is set to 6, and for CKD dataset, we set $K$ to 4.

**Evaluation Metrics** We assess the performance with three evaluation metrics: area under the receiver operating characteristic curve (AUROC), area under the precision-recall curve (AUPRC) and the minimum of precision and sensitivity (Min(P+Se)). Among those metrics, AUPRC is a more informative and primary metric when dealing with a highly imbalanced dataset like ours. [Davis and Goadrich, 2006]

**Baseline Methods** We select several state-of-the-art methods as our baselines. Baselines incorporating external medical knowledge are not included:

- GRU\(_a\) is the naive GRU with attention mechanism.
- RETAIN [Choi et al., 2016] (NeurIPS) applies different attention weights on different visits and medical features.
- T-LSTM [Baytas et al., 2017] (SIGKDD) tackles time intervals by introducing a time decay mechanism in LSTM. 
- TimeNet, [Gupta et al., 2018] (IJCAI) designs a shared encoder to embed all features respectively and learn correlations via linear layers. For fair comparison, pretraining is not conducted here.
- StageNet [Gao et al., 2020] (WWW) integrates patient disease stage development to learn feature correlations.
- ConCare [Ma et al., 2020] (AAAI) embeds each medical features individually, and employs self-attention mechanism to model and interpret feature correlations.

We also perform the following ablation studies:

- MedFACT\(_{cor}\) doesn’t consider any difference on feature correlations. The correlation graph is fully connected with all edge weights set to 1.
- MedFACT\(_{clu}\) doesn’t cluster features into groups. The correlation graph is fully connected, and the adjacency matrix $A$ equals to the correlation matrix $R$.

### 5.3 Experimental Results

Table 1 shows the performance of MedFACT and baselines on the two datasets. The value in (·) denotes the standard deviation of 1000-times bootstrapping and 5-fold cross-validation

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\(^1\)This study was approved by the Research Ethical Committee.
Table 1: Experimental Results for Tasks on Cardiology & CKD Datasets

| Methods | Mortality Prediction on CKD Dataset | Sepsis Prediction on Cardiology Dataset |
|---------|-----------------------------------|----------------------------------------|
|         | AUPRC | AUROC | Min(P+,Se) | AUPRC | AUROC | Min(P+,Se) |
| GRUα    | 0.6790(0.061) | 0.7849(0.041) | 0.6397(0.048) | 0.6356(0.030) | 0.9222(0.009) | 0.6389(0.024) |
| RETAIN  | 0.6938(0.053) | 0.8018(0.034) | 0.6744(0.027) | 0.7310(0.023) | 0.9386(0.008) | 0.6681(0.023) |
| T-LSTM  | 0.6976(0.056) | 0.8012(0.033) | 0.6670(0.049) | 0.6866(0.024) | 0.9258(0.009) | 0.6131(0.024) |
| TimeNetα| 0.7353(0.038) | 0.8219(0.024) | 0.6758(0.040) | 0.7829(0.020) | 0.9472(0.007) | 0.7004(0.022) |
| StageNet| 0.7301(0.029) | 0.8120(0.030) | 0.6729(0.057) | 0.7170(0.024) | 0.9421(0.007) | 0.6497(0.023) |
| ConCare | 0.7295(0.079) | 0.8226(0.039) | 0.6727(0.054) | 0.7740(0.021) | 0.9512(0.006) | 0.7037(0.021) |

Table 1: Experimental Results for Tasks on Cardiology & CKD Datasets

| Methods | Mortality Prediction on CKD Dataset | Sepsis Prediction on Cardiology Dataset |
|---------|-----------------------------------|----------------------------------------|
|         | AUPRC | AUROC | Min(P+,Se) | AUPRC | AUROC | Min(P+,Se) |
| MedFACT| 0.7469(0.048) | 0.8273(0.029) | 0.6786(0.034) | 0.7795(0.021) | 0.9522(0.006) | 0.7176(0.022) |
| MedFACT−cor | 0.7484(0.059) | 0.8323(0.034) | 0.6881(0.034) | 0.7823(0.021) | 0.9552(0.006) | 0.7146(0.021) |
| MedFACT−clu | 0.7653(0.039) | 0.8357(0.027) | 0.6921(0.046) | 0.8047(0.020) | 0.9556(0.006) | 0.7311(0.021) |

Figure 3: Performance comparison of MedFACT and several baselines with different amount of training data on Cardiology dataset.

for Cardiology and CKD dataset, respectively. As presented in Table 1, we observe that MedFACT significantly outperforms all other baselines on both datasets. This is mainly because it’s difficult for all the baselines (including ablation studies) to directly learn global feature correlations \( p(Z) \) from data, while MedFACT reduces it to several sub-problems, which lowers the learning complexity and brings improvements on performance. Especially for datasets with fewer samples, \( p(Z) \) is much harder to learn, and MedFACT can better mitigate this problem and reach higher performance. The conclusion gets proved on CKD dataset with much fewer patient samples. The relative performance boost reaches 4.08% on AUPRC and 1.59% on AUROC compared with the baseline, which is much larger than that on Cardiology dataset (2.78% on AUPRC and 0.46% on AUROC). Besides, comparing the two ablation studies, MedFACT−cor shows better performance than MedFACT−clu, indicating that it’s also effective to incorporate correlation differences in the model.

5.4 Analysis

Varying the Data Size We try to evaluate the robustness of MedFACT against insufficient training samples. Here we reduce the training set of Cardiology dataset from 80% to 30%/15%/10% of the whole dataset to simulate the scenario of data insufficiency, and the test set is fixed for a fair comparison. We conduct experiments on those different settings, and the AUPRC (± std.) is plotted in Figure 3. As is shown in Figure 3, MedFACT consistently outperforms all selected baselines under all settings. Furthermore, as the size of training set shrinks, the performances of other methods decrease more sharply than ours, leading to a larger performance gap. Even when we adopt only 10% of data for training, MedFACT still reaches an AUPRC of 0.6374, while MedFACT−cor and ConCare drop to 0.5866 and 0.5466, showing 8.66% and 16.6% relative improvement, respectively. Those results indicate that MedFACT is more tolerant of data insufficiency, and demonstrate the robustness of our method.

Varying the Number of Clusters \( K \) We try to observe the performance of MedFACT under different settings of \( K \) on CKD dataset. As is shown in Figure 4, the performance peaks at \( K = 4 \). Selecting a \( K \) that is too large or too small can lead to approximately 1% of performance decay. That’s because each cluster still contains lots of features if \( K \) is too small, making it hard to learn the group-wise correlations \( i.e., p(G_i|L) \). Meanwhile, if \( K \) is too large, there can be massive clusters but scarce features in each cluster, making the inter-group correlations \( i.e., p(L) \) hard to estimate.

Besides, it’s also interesting to analyze how feature clusters evolve as \( K \) increases. Figure 5 illustrates that the feature clusters gradually split up as \( K \) increases, and there are seldom features switched to another cluster when \( K \) changes, demonstrating the stability of our cluster results. The gradual split-up of clusters formulate a hierarchical structure of medical features, which can be concluded as medical knowledge obtained from data. Furthermore, the feature correlations in clusters are confirmed by medical literature. For example, [Jiang et al., 2020] shows positive correlations between albumin, SBP, and DBP in CKD patients, which matches cluster 4·1. This cluster is further split into two parts, one of which...
(i.e. cluster 6-1) is SBP and DBP, the blood pressure indicators. Another example is cluster 4-4. [Ellison, 2017] claims that electrolyte disorder is common in CKD patients, which can further lead to tissue edema and an increase of body weight. This exactly matches cluster 4-4, where K, Na, P are all features depicting electrolyte balance, and weight(Wgt) is also included. We also find that serum albumin(Alb), chloride(Cl), and appetite(Apt) are individually clustered after K = 6. Medical researches [Kubota et al., 2020; Grove et al., 2018; Menon et al., 2005] reveal that those features are all independent predictors of mortality in CKD, indicating that our model learns a more distinguishable representation space for those features.

6 Conclusion

In this paper, we propose a health representation learning framework MedFACT to reduce learning complexity while modeling medical feature correlations without external task-specific knowledge. MedFACT groups up features with strong correlations, and reduces global feature correlation estimation to several sub-problems estimating group-wise and inter-group correlations. Specifically, MedFACT designs a novel metric to cluster features, and construct a graph to learn feature correlations via GCNs. MedFACT demonstrates significant performance improvements, provides medical knowledge and discovers reasonable feature clusters that match medical literature. We hope MedFACT can provide valuable medical insights and help physicians better diagnose.

References

[Bai et al., 2018] Tian Bai, Shanshan Zhang, Brian L Egleston, and Slobodan Vucetic. Interpretable representation learning for healthcare via capturing disease progression through time. In Proceedings of the 24th ACM SIGKDD International Conference on Knowledge Discovery & Data Mining, pages 43–51, 2018.

[Baytas et al., 2017] Inci M Baytas, Cao Xiao, Xi Zhang, Fei Wang, Anil K Jain, and Jiayu Zhou. Patient subtyping via time-aware lstm networks. In Proceedings of the 23rd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining, pages 65–74. ACM, 2017.

[Choi et al., 2016] Edward Choi, Mohammad Taha Badhori, Jimeng Sun, Joshua Kulas, et al. Retain: An interpretable predictive model for healthcare using reverse time attention mechanism. In Advances in Neural Information Processing Systems, pages 3504–3512, 2016.

[Choi et al., 2017] Edward Choi, Mohammad Taha Badhori, Le Song, Walter F Stewart, and Jimeng Sun. Gram: graph-based attention model for healthcare representation learning. In Proceedings of the 23rd ACM SIGKDD international conference on knowledge discovery and data mining, pages 787–795, 2017.

[Davis and Goadrich, 2006] Jesse Davis and Mark Goadrich. The relationship between precision-recall and roc curves. In Proceedings of the 23rd international conference on Machine learning, pages 233–240. ACM, 2006.

[Ellison, 2017] David H Ellison. Treatment of disorders of sodium balance in chronic kidney disease. Advances in chronic kidney disease, 24(5):332–341, 2017.

[Gao et al., 2020] Junyi Gao, Cao Xiao, Yasha Wang, Wen Tang, et al. Stagenet: Stage-aware neural networks for health risk prediction. In Proceedings of The Web Conference 2020, pages 530–540, 2020.

[Gretton et al., 2012] Arthur Gretton, Karsten M Borgwardt, Malte J Rasch, Bernhard Schölkopf, and Alexander Smola. A kernel two-sample test. The Journal of Machine Learning Research, 13(1):723–773, 2012.

[Grove et al., 2018] Birgith Engest Grove, Liv Marit Schougaard, Niels Henrik Hjollund, and Per Iversen. Self-rated health, quality of life and appetite as predictors of initiation of dialysis and mortality in patients with chronic kidney disease stages 4–5: a prospective cohort study. BMC research notes, 11(1):1–6, 2018.

[Gupta et al., 2018] Priyanka Gupta, Pankaj Malhotra, Lovekesh Vig, and Gautam Shroff. Using features from pre-trained timenet for clinical predictions. In The 3rd International Workshop on Knowledge Discovery in Healthcare Data at IJCAI, 2018.

[Harbarth et al., 2001] Stéphane Juergen Harbarth, K Holeckova, C Froidevaux, et al. Diagnostic value of procalcitonin, interleukin-6, and interleukin-8 in critically ill patients admitted with suspected sepsis. American Journal of Respiratory and Critical Care Medicine, 164(3):396–402, 2001.
[Jiang et al., 2020] Chongfei Jiang, Binyan Wang, Youbao Li, Liling Xie, et al. U-shaped association between serum albumin and development of chronic kidney disease in general hypertensive patients. *Clinical Nutrition*, 39(1):258–264, 2020.

[Kamal, 2014] Azra Kamal. Estimation of blood urea (bun) and serum creatinine level in patients of renal disorder. *Indian J Fundam Appl Life Sci*, 4(4):199–202, 2014.

[Kipf and Welling, 2016] Thomas N Kipf and Max Welling. Semi-supervised classification with graph convolutional networks. *arXiv preprint arXiv:1609.02907*, 2016.

[Kubota et al., 2020] Keiichi Kubota, Yusuke Sakaguchi, Takayuki Hamano, et al. Prognostic value of hypochloremia versus hyponatremia among patients with chronic kidney disease-a retrospective cohort study. *Nephrology Dialysis Transplantation*, 35(6):987–994, 2020.

[Lu et al., 2021] Chang Lu, Chandan K Reddy, Prithwish Chakraborty, Samantha Kleinberg, and Yue Ning. Collaborative graph learning with auxiliary text for temporal event prediction in healthcare. *arXiv preprint arXiv:2105.07542*, 2021.

[Ma et al., 2018] Fenglong Ma, Quanzeng You, Houping Xiao, Radha Chitta, Jing Zhou, and Jing Gao. Kame: Knowledge-based attention model for diagnosis prediction in healthcare. In *Proceedings of the 27th ACM International Conference on Information and Knowledge Management*, pages 743–752, 2018.

[Ma et al., 2020] Liantao Ma, Chaohe Zhang, Yasha Wang, Wenjie Ruan, Jiayu Zhou, et al. Concare: Personalized clinical feature embedding via capturing the healthcare context. In *Proceedings of the AAAI Conference on Artificial Intelligence*, volume 34, pages 833–840, 2020.

[Menon et al., 2005] Vandana Menon, TOM Greene, Xuelei Wang, Arema A Pereira, Santica M Marcovina, et al. C-reactive protein and albumin as predictors of all-cause and cardiovascular mortality in chronic kidney disease. *Kidney international*, 68(2):766–772, 2005.

[Reyna et al., 2019] Matthew A Reyna, Chris Josef, Salman Seyed, Russell Jeter, et al. Early prediction of sepsis from clinical data: the physionet/computing in cardiology challenge 2019. In *2019 Computing in Cardiology (CinC)*, pages Page–1. IEEE, 2019.

[Song et al., 2018] Huan Song, Deepta Rajan, Jayaraman J Thiagarajan, and Andreas Spanias. Attend and diagnose: Clinical time series analysis using attention models. In *32nd AAAI conference on artificial intelligence*, 2018.

[Stella and Shi, 2003] X Yu Stella and Jianbo Shi. Multi-class spectral clustering. In *Computer Vision, IEEE International Conference on*, volume 2, pages 313–313. IEEE Computer Society, 2003.

[Zhang et al., 2019] Xi Sheryl Zhang, Fengyi Tang, Hiroko H Dodge, Jiayu Zhou, and Fei Wang. Metapred: Meta-learning for clinical risk prediction with limited patient electronic health records. In *Proceedings of the 25th ACM SIGKDD International Conference on Knowledge Discovery & Data Mining*, pages 2487–2495, 2019.
### Table 1: Statistics of Datasets

| Dataset       | CKD     | Cardiology |
|---------------|---------|------------|
| # of patients | 662     | 40,336     |
| # of visits   | 13,108  | 1,552,210  |
| Avg. visits / patient | 19.95  | 38.48      |
| Max. visits / patient | 69     | 336        |
| Min. visits / patient | 1      | 8          |
| # of dynamic features | 17     | 34         |
| # of static features  | 4      | 5          |
| % of positive labels | 38.97%  | 7.26%      |

### Table 2: Features Recorded in CKD and Cardiology Dataset

| CKD Features | Cardiology Features |
|--------------|---------------------|
| Systolic BP  | Heart Rate          |
| Diastolic BP | Temperature         |
| Urea         | Diastolic BP        |
| Calcium      | MAP                 |
| Chloride     | Resp. Rate          |
| Creatinine   | EtCO₂               |
| Phosphate    | BaseExcess          |
| Potassium    | FiO₂                |
| Hemoglobin   | PaCO₂               |
| WBC Count    | FiO₂                |
| Sodium       | pH                  |
| CO₂CP        | AST                 |
| Albumin      | SaO₂                |
| Weight       | Calcium             |
| Appetite     | Chloride            |
| hs-CRP       | Creatinine          |
|             | Dir. Bilirubin      |
| Static       | Age                 |
| Gender       | Lactate             |
| Height       | Magnesium           |
| Diabetes     | Phosphate           |
|              | Tot. Bilirubin      |
|              | TroponinI           |
|              | Hematocrit          |
|              | Hemoglobin          |
|              | PTT                 |
|              | WBC Count           |
|              | Fibrinogen          |
|              | Platelets           |
|              | HospAdmTime         |

### Dataset Statistics

In this section, we introduce the dataset we use (i.e. CKD dataset and Cardiology dataset) in experiments in detail. Specifically, CKD dataset is recorded with chronic patients, and their visits are generated monthly. Cardiology dataset only consists of ICU patients, and the visits are recorded hourly. We present the detailed statistics in Table 1, and all the dynamic and static medical features are listed in Table 2.

### Varying Number of Clusters \( K \) on Cardiology Dataset

We have already studied how number of clusters \( K \) affects the performance of MedFACT on CKD dataset in our main text. Here we also provide similar analysis on Cardiology dataset. Figure 1 shows the performance of MedFACT under different settings of \( K \). The results indicate the same conclusions as CKD that selecting a \( K \) too large or too small will make it challenging to learn group-wise or inter-group feature distributions \( p(G_i|Z) \) or \( p(Z) \) and lead to performance decay. Here we present a possible intuitive approach to select a better \( K \) which may balance the learning complexity of \( p(G_i|Z) \) and \( p(Z) \). Assume that the learning complexity of \( p(G_i|Z) \) is a function of the number of features in each group (i.e. \( \phi(F/K) \)), and the learning complexity of \( p(Z) \) is a function of the number of clusters (i.e. \( \phi(K) \)). Then the balance of learning complexity is achieved when \( F/K = K \), which is \( K = \sqrt{F} \). This provides an intuitive approximation of \( K \) for better performance. As a result, \( K \) is set to \( 6 \approx \sqrt{34} \) for Cardiology dataset, and \( K \) is \( 4 \approx \sqrt{17} \) for CKD dataset, and the performances reach their peak at those settings.