Capturing Feature-Level Irregularity in Disease Progression Modeling

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NUHS National University Health System

Outline

- Introduction
- Existing Solutions for Irregularity
- Problem Definition
- Methodology
- Evaluation
- Case Study
- Conclusion

Introduction

Chronic Diseases

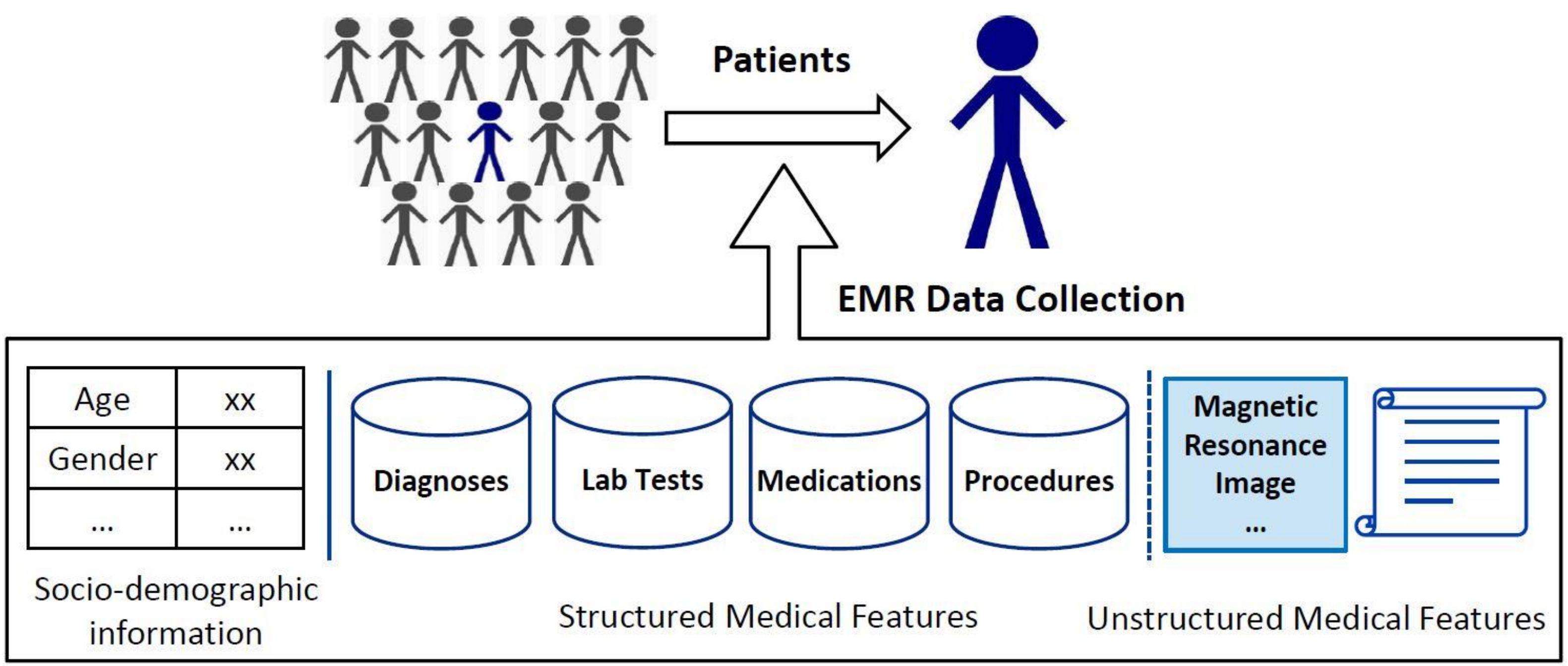
- Major cause of illnesses and deaths
- Likely to worsen with more severe comorbidities and complications without intervention

Disease Progression Modeling (DPM)

- Employ computational methods to model the progression of a target disease
- Facilitate early detection and treatment of chronic diseases before deterioration
- Exploit electronic medical records (EMR) for analytics

Introduction

Electronic Medical Records (EMR)



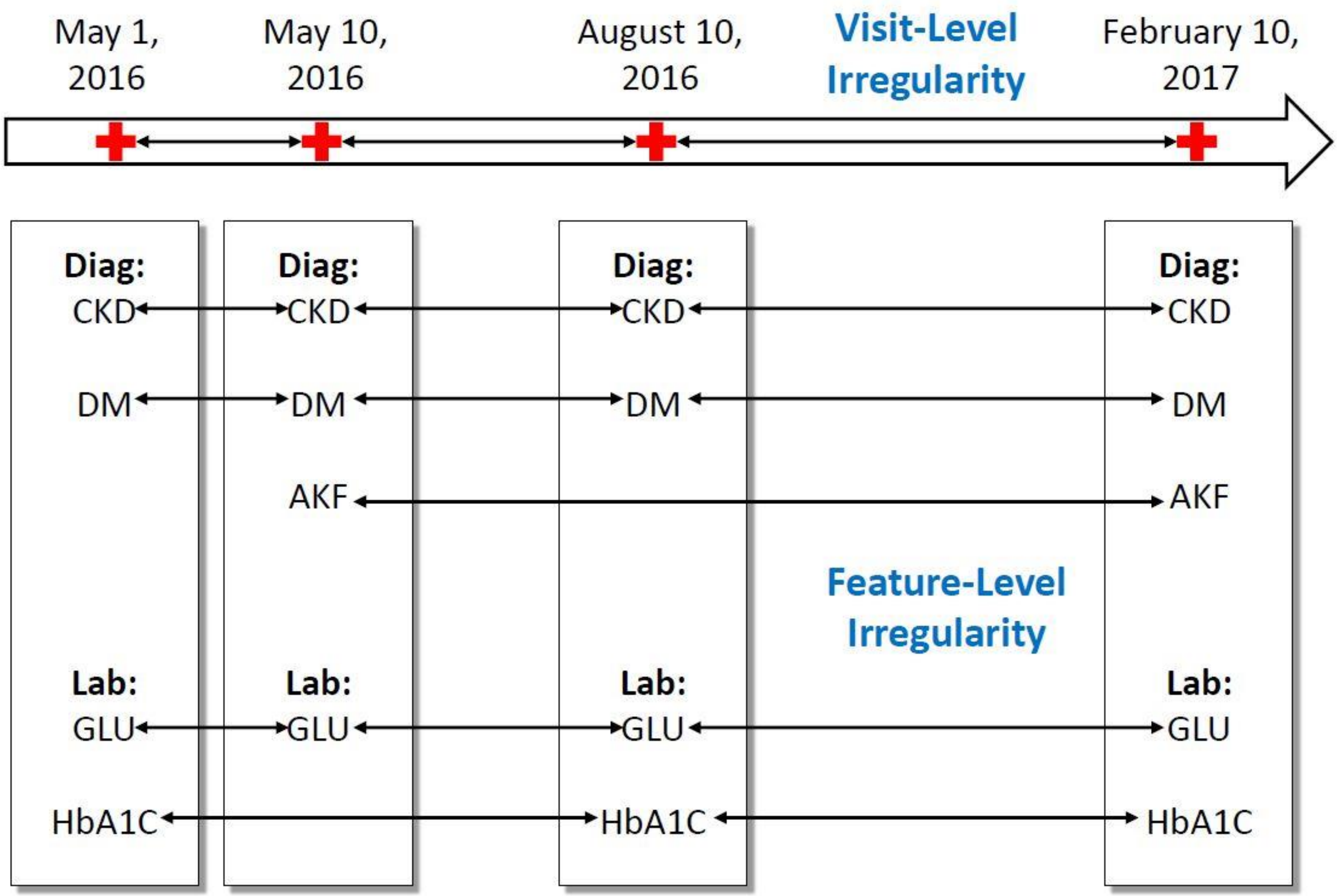
Introduction

Electronic Medical Records (EMR)

- One major challenge of DPM over EMR data is on handling the **irregularity** issue of the time series EMR data
- Two levels: visit-level irregularity, feature-level irregularity
  - Visit-Level Irregularity
    - EMR data appears irregularly with time
    - Time span between consecutive visits is irregular
  - Feature-Level Irregularity
    - Same feature appears irregularly in EMR data with time
    - Time span between a feature's consecutive occurrences is irregular

Introduction

Electronic Medical Records (EMR)



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Existing Solutions for Irregularity

I. Converting to Non-Time Series Data

(Duchesne et al., 2009; Stonnington et al., 2010; Zhou et al., 2011; Zhou et al., 2012)

☺ simple computation and modeling

☹ under-utilization of time series EMR data

II. Transforming into Regular Time Series Data

- Dynamic Bayesian networks or variant graphical models

(Van Gerven et al., 2008; Exarchos et al., 2013; Wang et al., 2014)

☺ causality and interpretability

☹ time-consuming & need experts' domain knowledge

- Deep learning models

(Che et al., 2014; Che et al., 2015; Lipton et al., 2016)

☺ better performance in many areas for feature learning

☹ difficult to capture feature patterns within a time window

Existing Solutions for Irregularity

III. Without Transforming Data

- Input EMR data of patients' visits in chronological order without considering the intrinsic irregularity (Choi et al., 2016)
- Utilize irregular EMR data by concatenating the visits' timestamps in the inputs (Choi et al., 2016)
- Use the time span as a visit-level decay term to analyze EMR data (Pham et al., 2016)

  ☺ incorporate all visit-level information available

  ☹ not use feature-wise time span or distinguish various features

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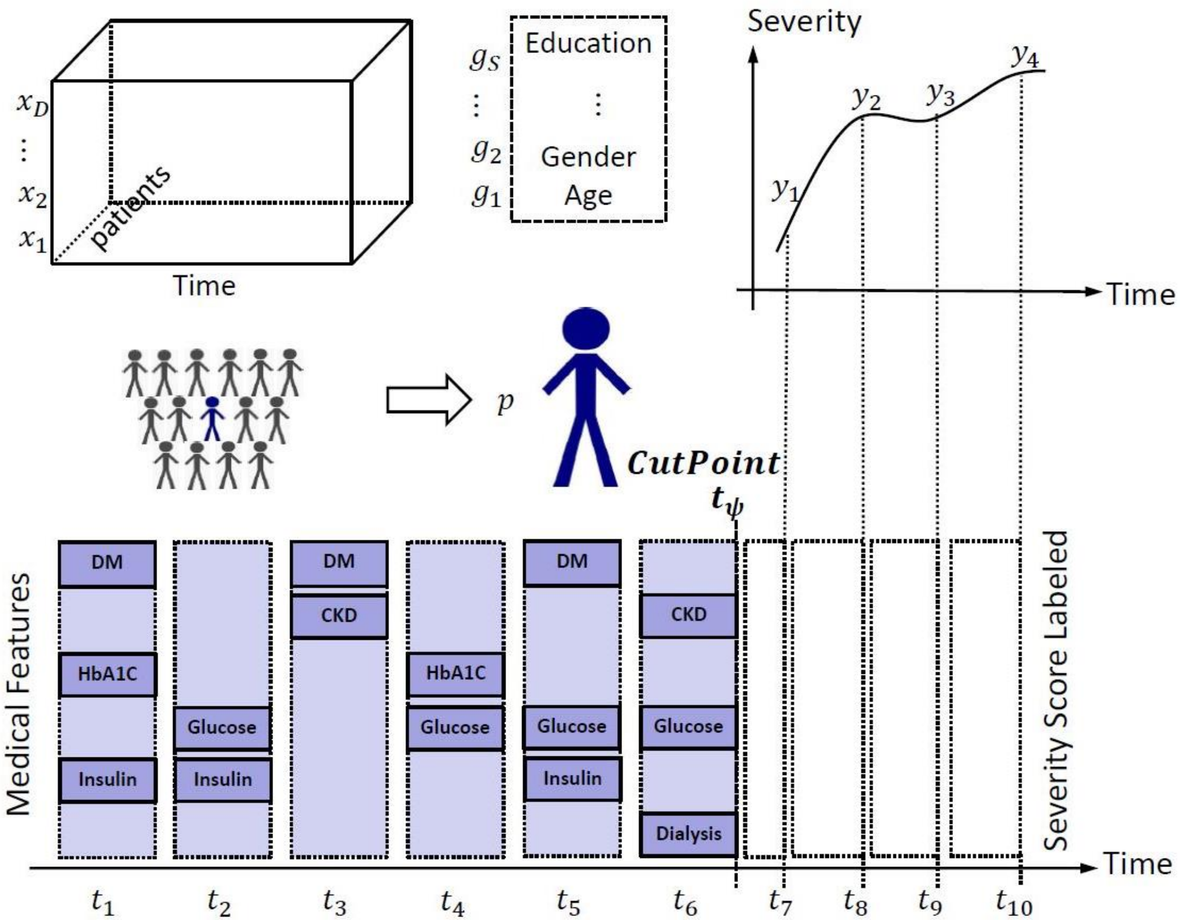
Problem Definition



Disease Progression Modeling (DPM)

Given a set of training samples $\{< x, y, \Delta t >\}$, the objective of DPM is to obtain a mapping function Φ that minimizes the following loss function over all samples: $L(\Phi(x, \Delta t), y)$

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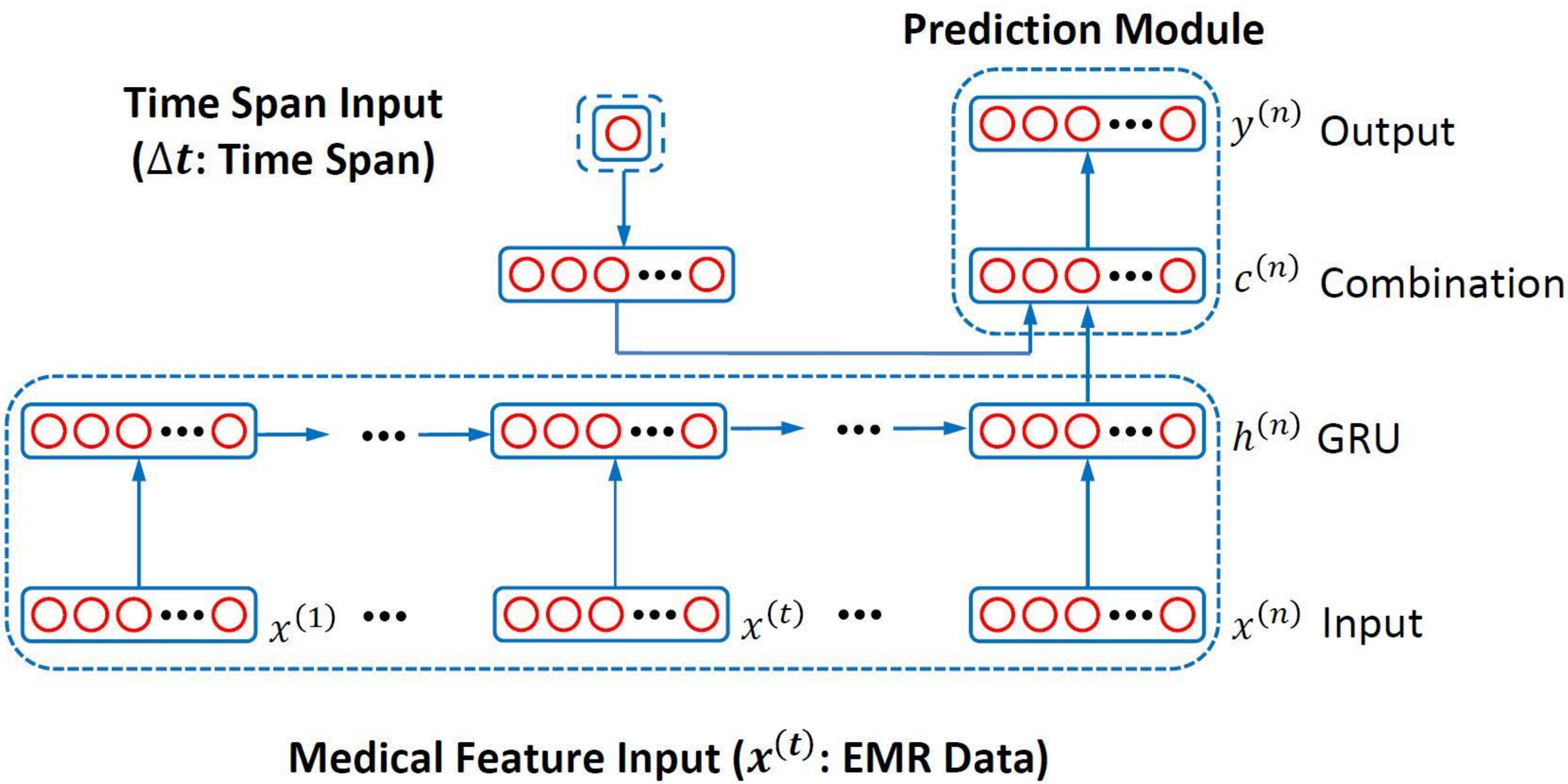
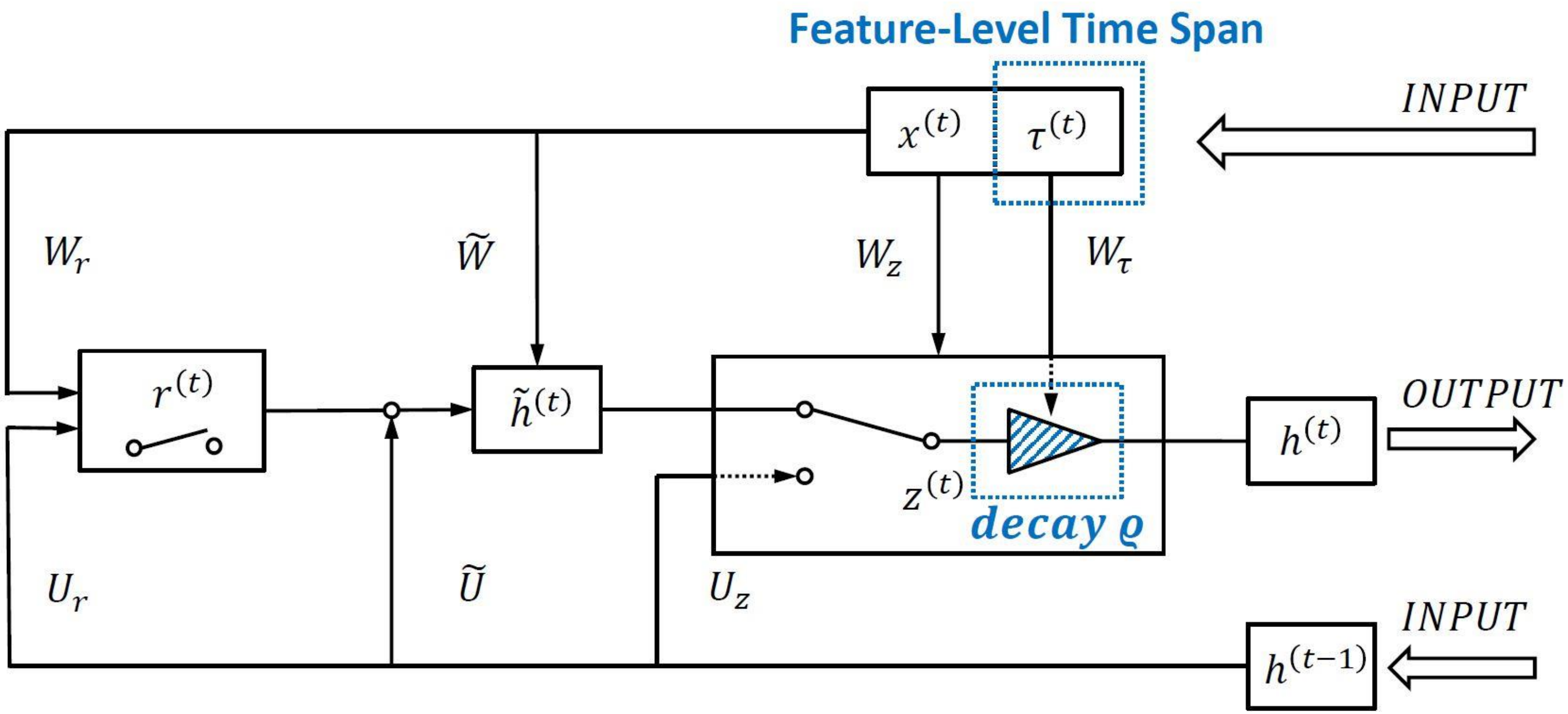
Methodology



Loss function: $L = \frac{1}{|\{<x,y,\Delta t>\}|}\sum\left(y^{(n)} - y\right)^2$

Back-propagation algorithm for updating the model parameters

Methodology



Compute a decay term ϱ using $\tau(t)$ and multiply ϱ to $z(t)$

- $\varrho = 1 - tanh\left(W_\tau \tau^{(t)} + b_\tau\right)$
- $z(t) = sigmoid\left(\left(W_z x^{(t)} + U_z h^{(t-1)}\right) \odot \varrho\right)$

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Evaluation

ADNI dataset

- Public Alzheimer's disease dataset from Alzheimer's Disease Neuroimaging Initiative
- Severity is measured by Mini-Mental State Examination (MMSE) test ($\in [0,30]$)

NUH-CKD dataset

- Extract from a chronic kidney disease (CKD) dataset from National University Hospital in Singapore
- Choose patients with Stage 3 CKD or higher as cohort, "NUH-CKD" dataset
- Severity is measured by Glomerular Filtration Rate (GFR) test ($\in [0,60]$)

Evaluation metrics

- Mean squared error (MSE)
- Pearson product-moment correlation coefficient (R) value

Evaluation

Dataset	ADNI1 Dataset	NUH-CKD Dataset
# of medical features	591	603
# of demo. features	3 — age, gender, education time	2 — age, gender
# of patients	819	2740
Time span	4 years, M00 to M48, ("M" — "month")	1 year, W00 to W52, ("W" — "week")
# of time steps	7 (aggregated by every 6 months)	52 (aggregated by every week)
CutPoint (t_ψ) setting	M12, M18, M24	W16, W24, W32
# of samples	t_ψ=M12: 1529 t_ψ=M18: 1200 t_ψ=M24: 558	t_ψ=W16: 3601 t_ψ=W24: 2793 t_ψ=W32: 1585

Evaluation

GRU-based baselines

- Window-Based Model
- Visit-Level Model
- Visit-Level Time Decay Model

Multi-task learning (MTL) methods (Zhou et al., 2012)

- Least Convex Fused Group Lasso (cFSGL)
- Least Non-Convex Fused Group Lasso (nFSGL), denote two formulations as nFSGL-1 and nFSGL-2 in experiments

Our proposed method

- Feature-Level Time Decay Model

Evaluation

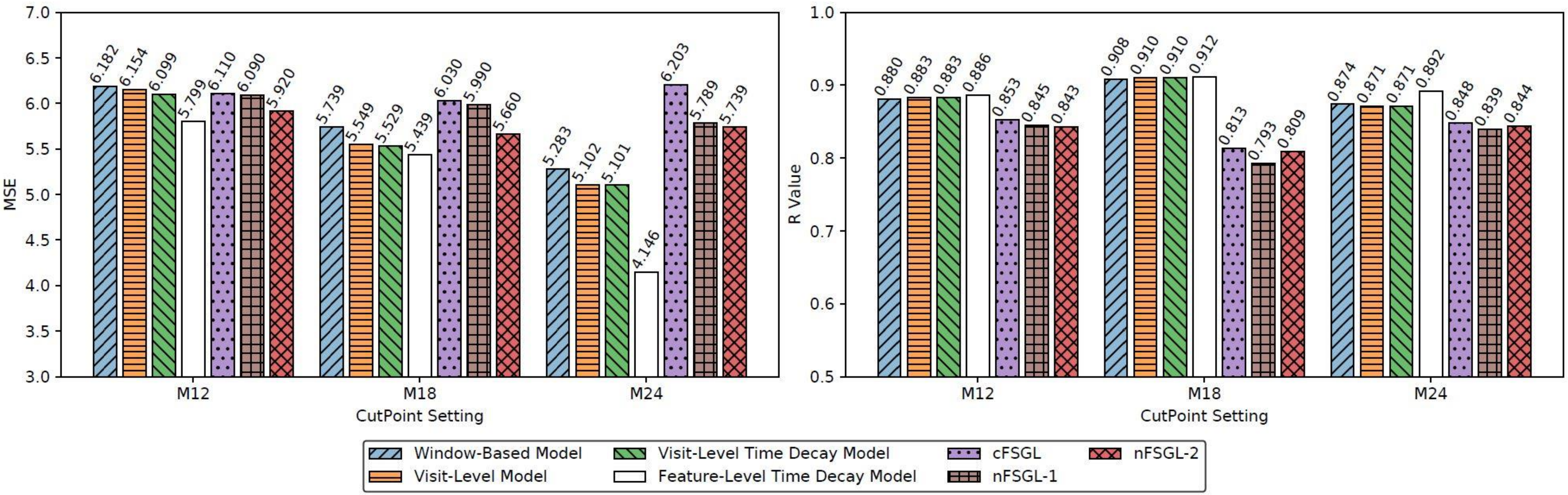

Figure: Experimental results in the ADNI dataset

- For the same CutPoint setting, from Window-Based Model to Feature-Level Time Decay Model, performance is mainly on the ascending trend; Feature-Level Time Decay Model more accurate than MTL-based methods;
- When CutPoint becomes larger, MSE values of GRU-based models decrease

Evaluation

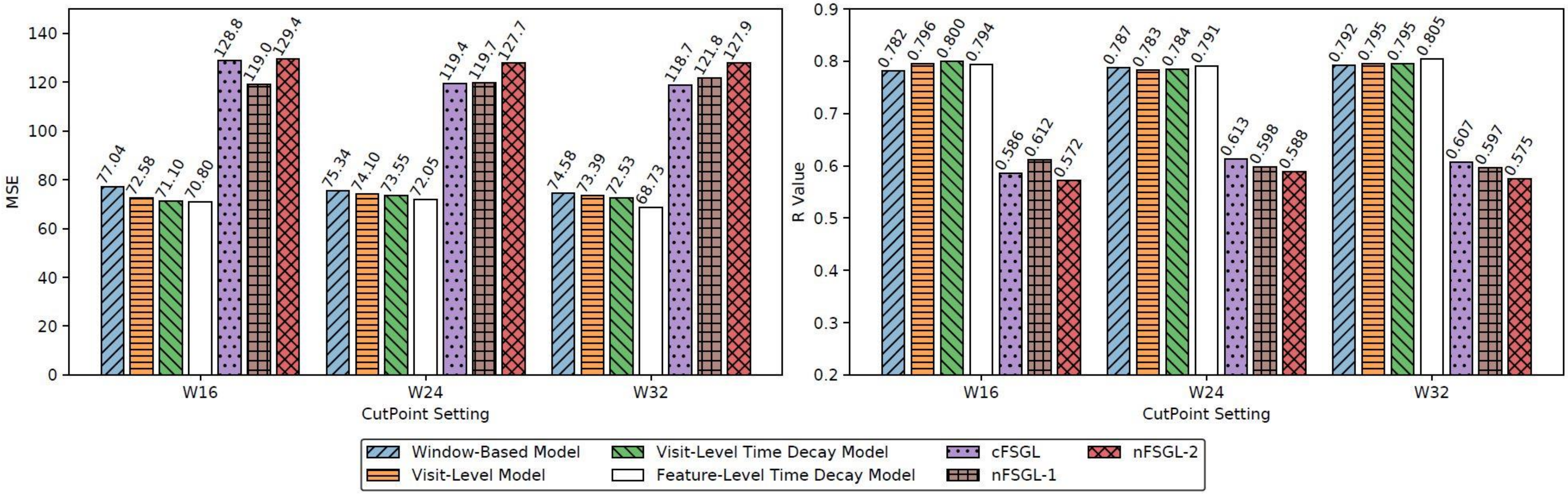

Figure: Experimental results in the NUH-CKD dataset

- From W16 to W24, GRU-based models achieve larger MSE values **- decreasing number of samples**
- From W24 to W32, GRU-based models achieve smaller MSE values **- more time series features**
- Both the sample length and sample number affect the model performance

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Case Study – Patient1

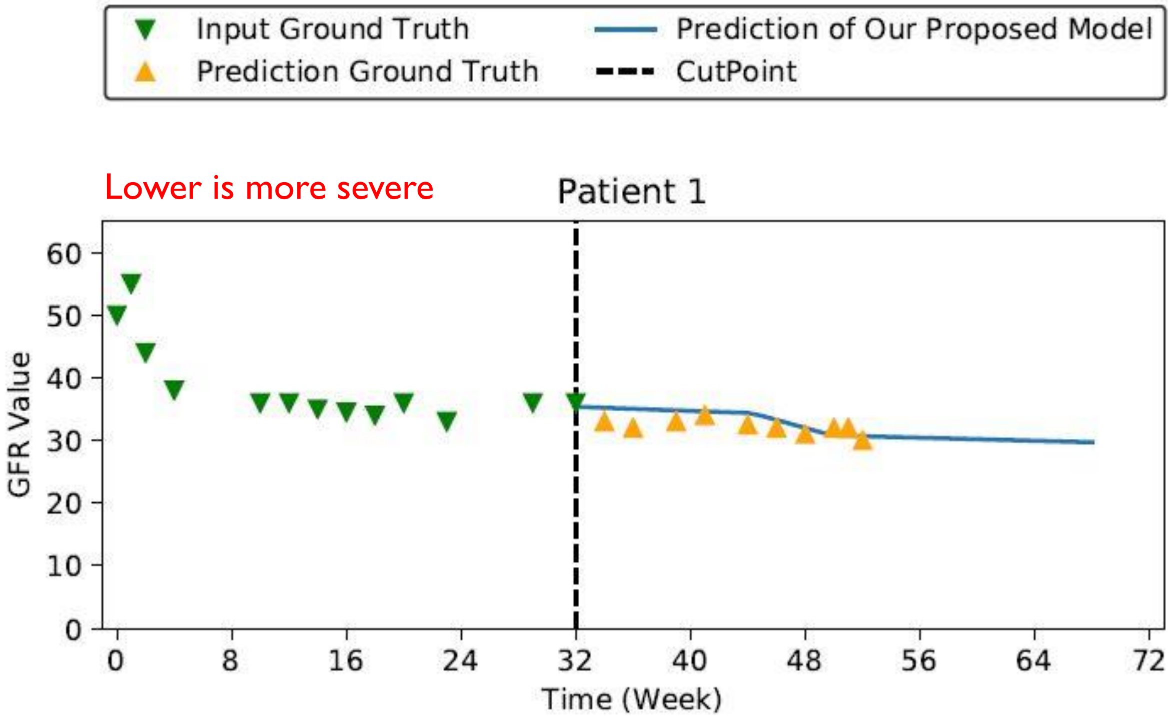

Figure: Disease progression modeling illustration for representative CKD Patient1 in the NUH-CKD dataset

Severe and deteriorating

- GFR decreases in the first 32 weeks and drops to around 35
- From the 32nd week, GFR remains in the descending trend
- Furthermore, our proposed model predicts that as time further goes on, the loss of Patient1's GFR will exceed 5ml/min/1.73m^2 within one year

- Our model would suggest Patient1 to consult specialists for expert assessment

Case Study – Patient2

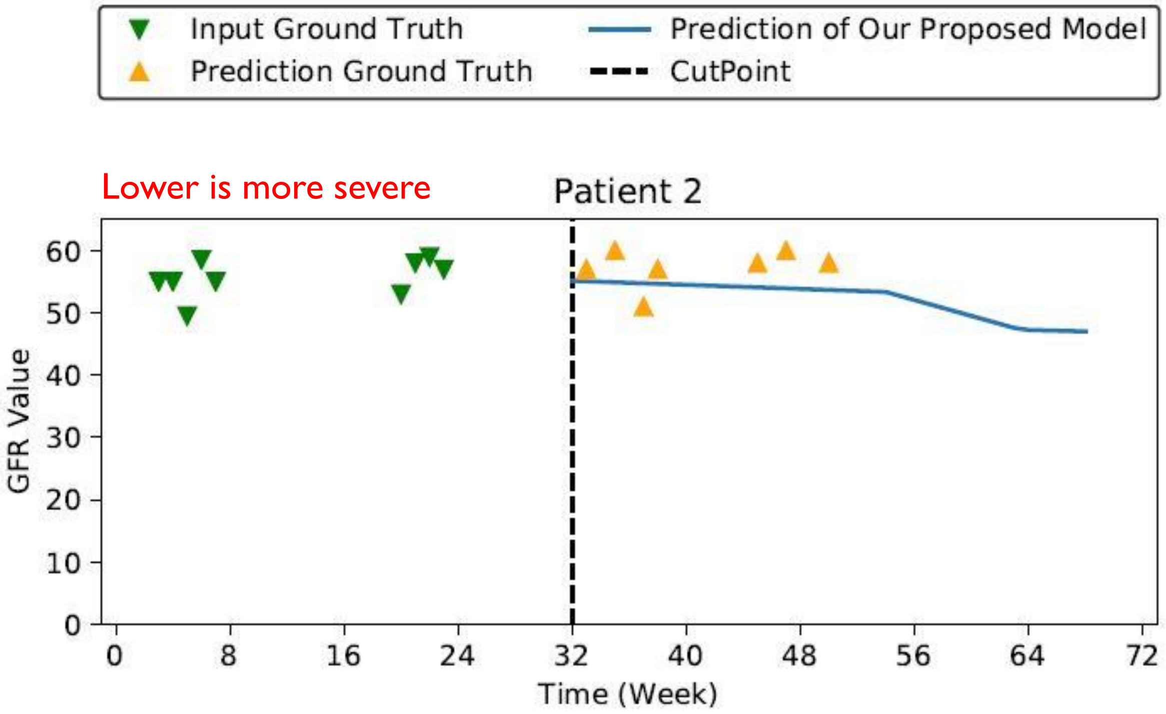

Figure: Disease progression modeling illustration for representative CKD Patient2 in the NUH-CKD dataset

Mild yet deteriorating

- In the beginning, GFR indicates only moderately reduced kidney function. However, GFR decreases slowly over time before the 52nd week
- After the 52nd week, our model predicts that the patient will suffer from a large drop in GFR, indicating the deterioration of kidney functioning

- Our model would suggest healthcare workers to provide more aggressive interventions to Patient2 in advance

Case Study – Patient3

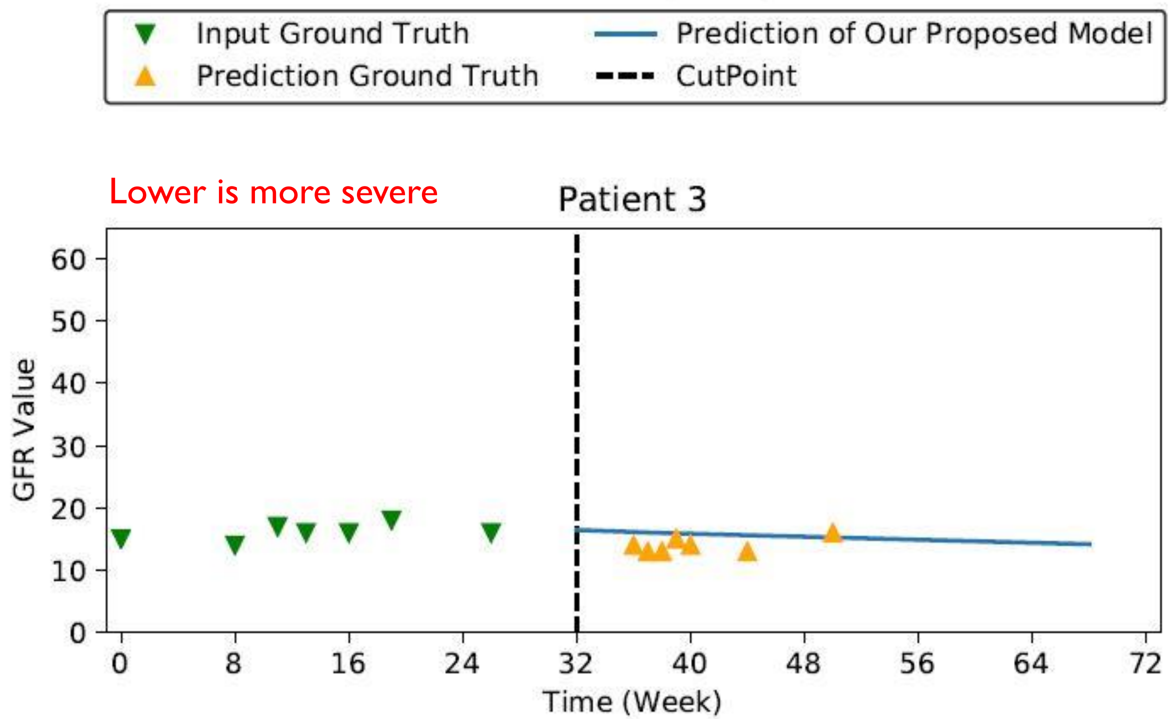

Figure: Disease progression modeling illustration for representative CKD Patient3 in the NUH-CKD dataset

Severe yet stable

- Patient3 is already in CKD Stage5 in the beginning
- Through the whole year, this patient progresses stably without much change in GFR
- Our model gives the prediction that this stableness will maintain for a long time

- Our model would suggest guaranteeing the monitoring for Patient3

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Conclusion

I. ***Identify the irregularity characteristic residing in EMR data both at the visit level and at the feature level***

II. ***Capturing feature-level irregularity can benefit EMR data analytics through Feature-Level Time Decay Model***

- Handle feature-level irregularity
- Decay the influence of previous information on patients' current state
- Learn decaying parameters for different features

III. ***Evaluate proposed Feature-Level Time Decay Model in both a public ADNI dataset and a private NUH-CKD dataset for two chronic disease cohorts***

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Thank you!

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