

Motivation

- Time-series modeling is a ubiquitous task across many domains. We aim to create a powerful non-linear latent variable model of time-series.
- Patient records are a time series of diagnoses, lab tests, surgical procedures and drug prescriptions that represent observations of underlying conditions.
- What is the best treatment course for a patient? Which patients are similar to a given patient? Which policy is the most cost effective for a specific population? The wide availability of Electronic Health Records (EHR) gives machine learning the potential for addressing these questions.

Background

Kalman Filters Generative time series models are characterized by their **action transition** functions and their **emission** functions. Classic Kalman filters use linear functions for both:

$$z_t \sim \mathcal{N}(G \cdot z_{t-1} + B \cdot u_{t-1}, \Sigma) \quad (\text{action transition})$$

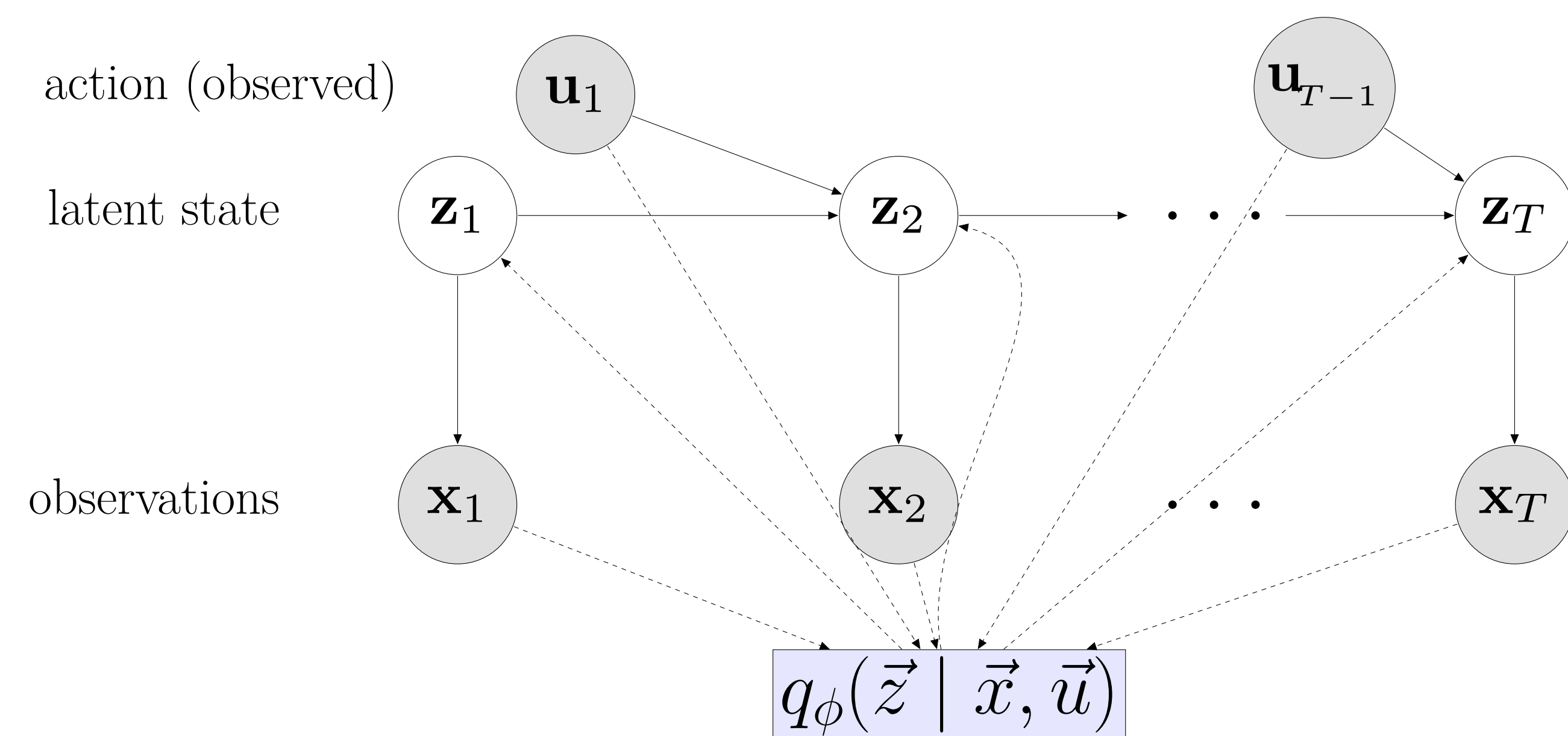
$$x_t \sim \mathcal{N}(F \cdot z_t, \Gamma) \quad (\text{emission})$$

Stochastic Backpropagation Rezende *et al.* (2014) and Kingma & Welling (2013) proposed using a neural net as a variational autoencoder to optimize a lower-bound on the model log-likelihood:

Counterfactual Inference “What would the patient’s blood sugar level be had she taken a different medication?”

Probabilistic Model

Variational autoencoder applied to the Kalman filter time-series model



We apply **stochastic backpropagation** to learn a **non-linear Kalman filter**, and use the model to perform **counterfactual inference**.

$$z_t \sim \mathcal{N}(G_\alpha(z_{t-1}, u_{t-1}), S_\beta(z_{t-1}, u_{t-1})) \quad (\text{action transition})$$

$$x_t \sim p(x_t | z_t; F_\kappa(z_t)) \quad (\text{emission})$$

G_α , S_β and F_κ are functions parameterized by neural nets

Proposition

For the graphical model we propose, the posterior factorizes as:

$$p(\vec{z} | \vec{x}, \vec{u}) = p(z_1 | \vec{x}, \vec{u}) \prod_{t=2}^T p(z_t | z_{t-1}, x_t, \dots, x_T, u_{t-1}, \dots, u_{T-1})$$

Approximating the Evidence Lower Bound

The recognition model prior q_ϕ is parameterized by a neural network ϕ . We use the prior factorization:

$$q_\phi(\vec{z} | \vec{x}, \vec{u}) = \prod_{t=1}^T q_\phi(z_t | z_{t-1}, x_t, \dots, x_T, \vec{u})$$

We maximize the following variational lower bound for training the generative and recognition models:

$$\log p_\theta(\vec{x} | \vec{u}) \geq \mathcal{L}(x; (\theta, \phi)) =$$

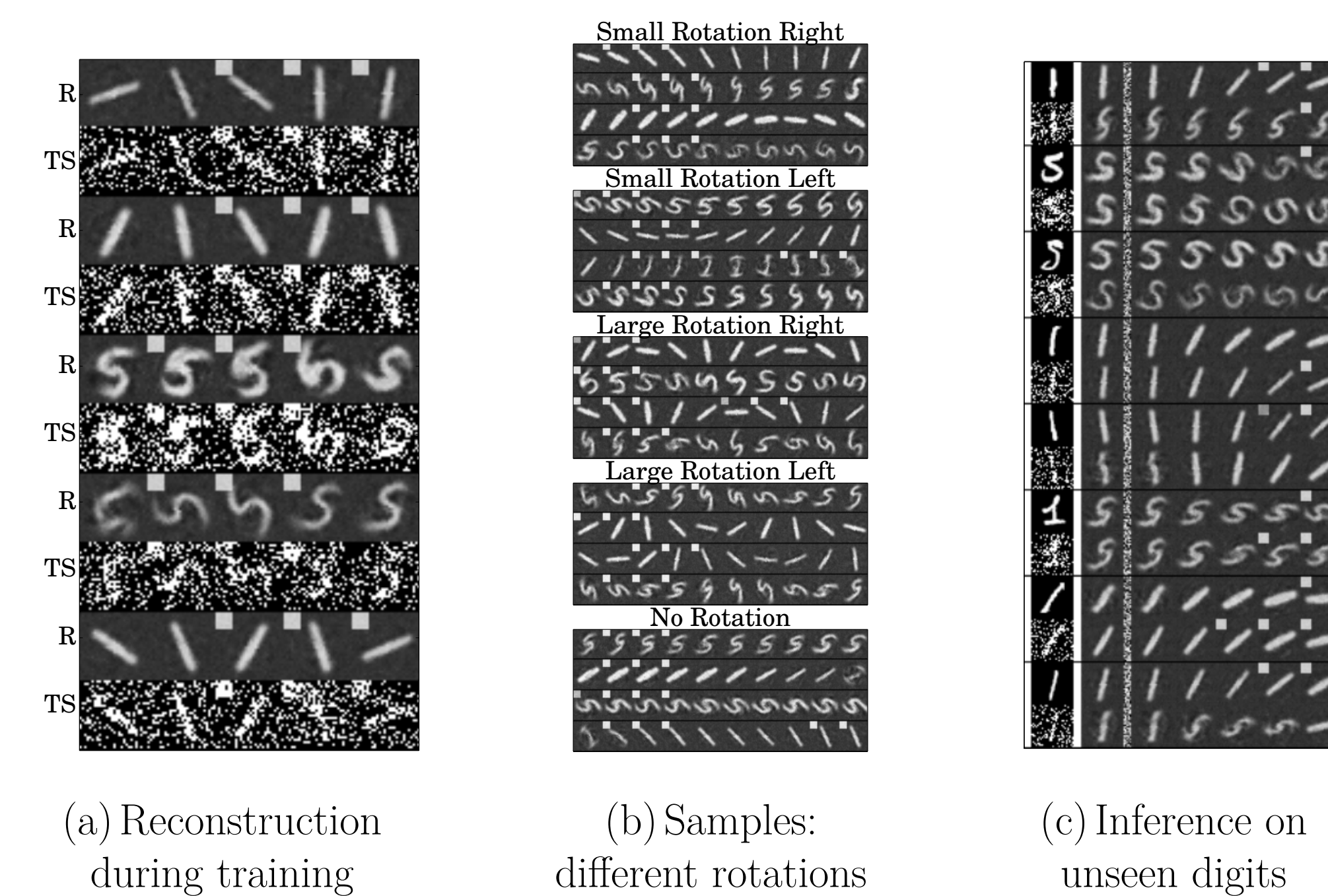
$$\sum_{t=1}^T \mathbb{E}_{q_\phi(z_t | \vec{x}, \vec{u})} [\log p_\theta(x_t | z_t)] - \text{KL}(q_\phi(z_1 | \vec{x}, \vec{u}) || p_0(z_1))$$

$$- \sum_{t=2}^T \mathbb{E}_{q_\phi(z_{t-1} | \vec{x}, \vec{u})} [\text{KL}(q_\phi(z_t | z_{t-1}, \vec{x}, \vec{u}) || p_0(z_t | z_{t-1}, u_{t-1}))].$$

Experiments

Healing MNIST

Sequences of MNIST digits, where the action is a digit being rotated. We add random noise, and structured noise in the form of a block on the top-left corner place on three consecutive digits within the sequence.



Recognition Models

q-INDEP: (7 layer MLP)

$$q(z_t | x_t, u_t)$$

q-LR: (7 layer MLP)

$$q(z_t | x_{t-1}, x_t, x_{t+1}, u_{t-1}, u_t, u_{t+1})$$

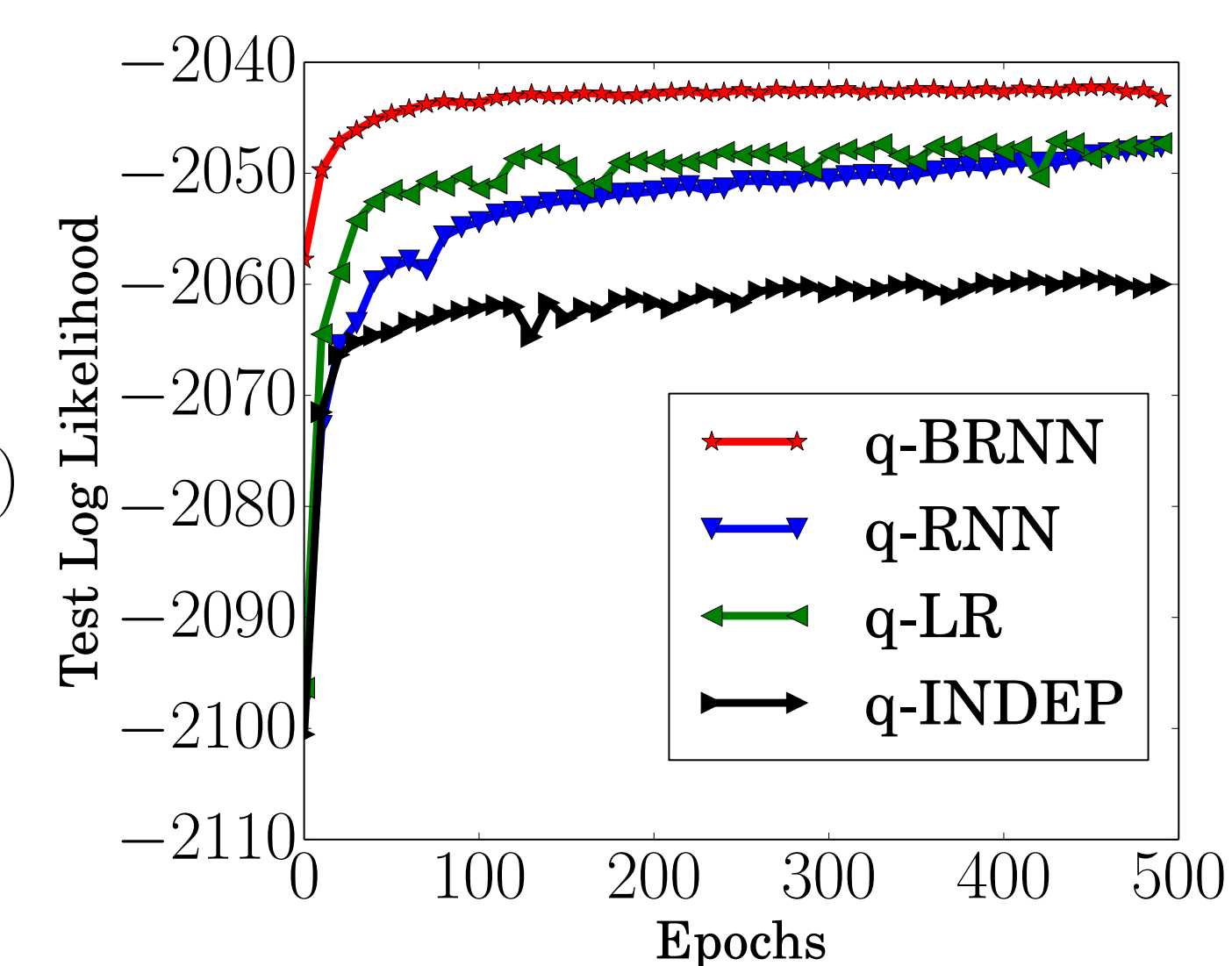
q-RNN: (2 layer MLP + 2 layer RNN)

$$q(z_t | x_1, \dots, x_t, u_1, \dots, u_t)$$

q-BRNN:

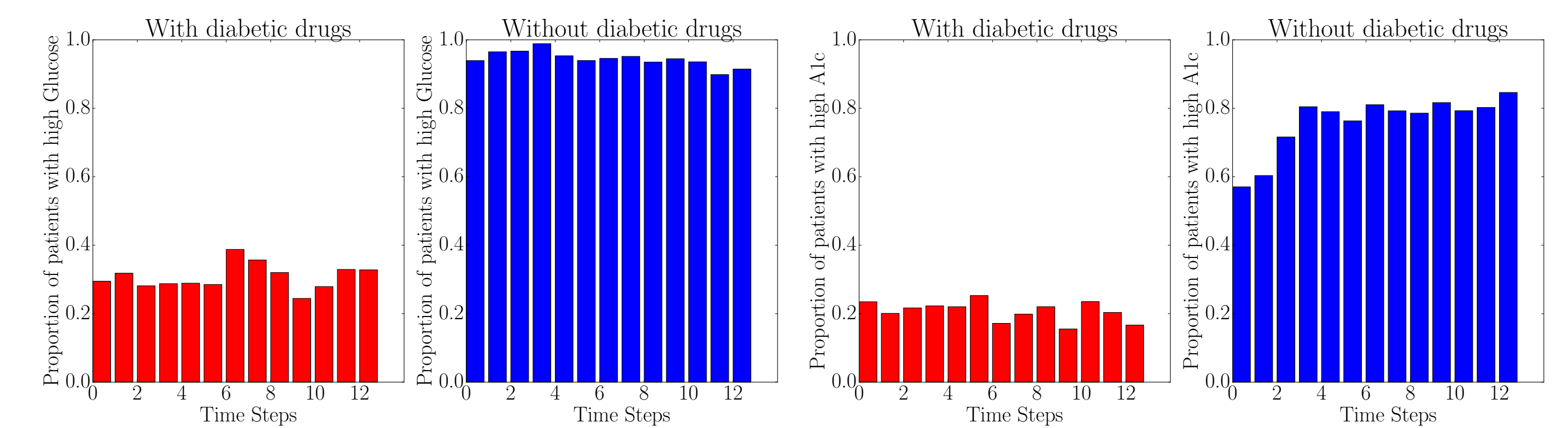
(2 layer MLP + 2 layer bi-RNN)

$$q(z_t | x_1, \dots, x_T, u_1, \dots, u_T)$$



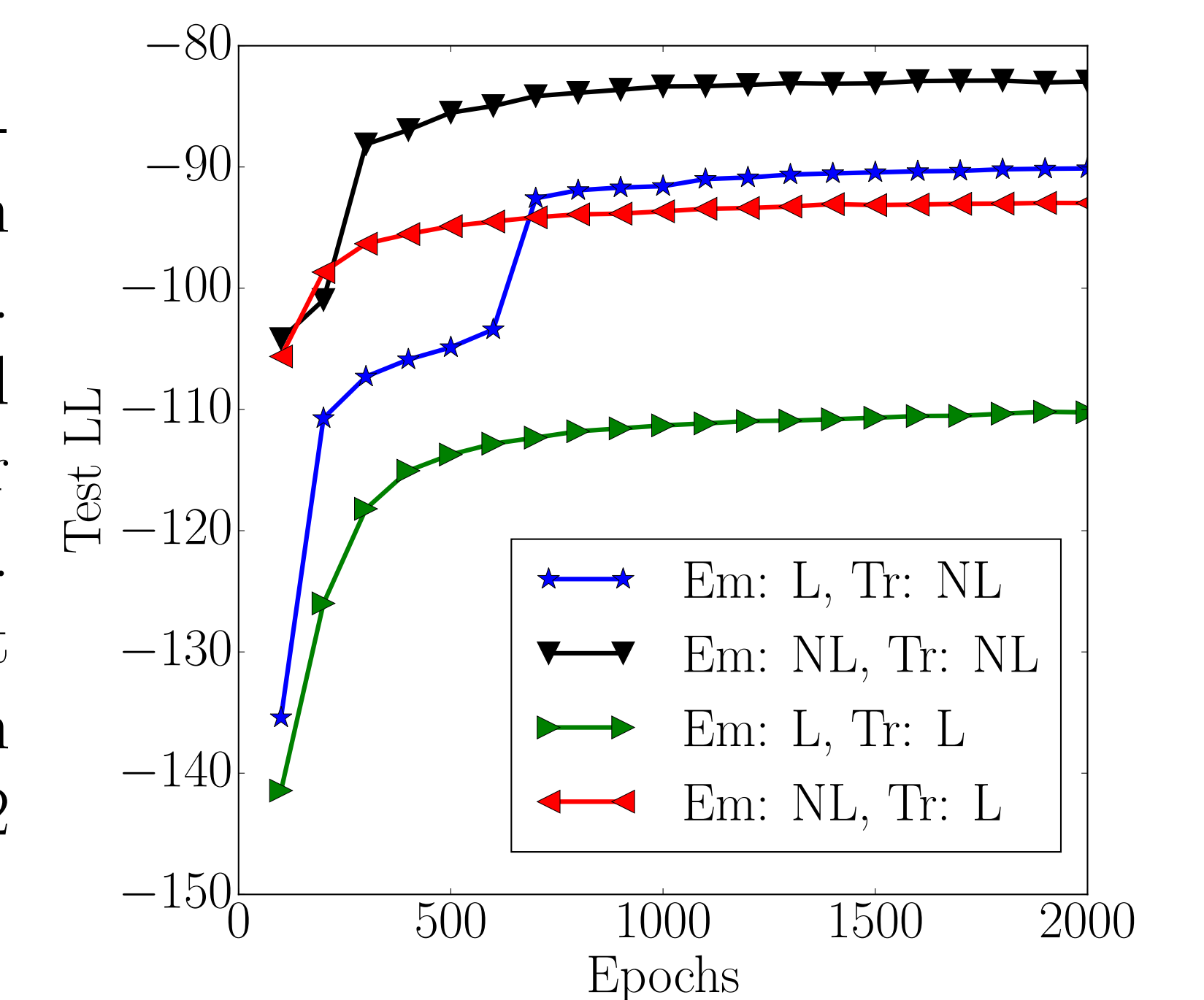
Medical Data

- Healthcare records data of 8000 diabetic and pre-diabetic patients.
- Infer future lab test values of A1c and glucose in counterfactual scenarios.
- Patient data: age, gender, and ICD-9 diagnoses code depicting comorbidities such as heart failure, kidney conditions or obesity.



Proportion of patients with high Glucose Proportion of patients with high A1c

Test log-likelihood for different models. Em: emission model. Tr: transition model. L: linear. NL: non-linear. All non-linear models are 3-layer fully connected ReLU units. The dimension of the latent space z_t is 30. Recognition model is a 2 layer MLP + 2 layer bi-directional RNN.



Sample Patient. The x-axis denotes time and the y-axis denotes the observations. The patient was sampled under no medication. The intensity of the colour denotes its value between zero and one.