Probabilistic Modelling of Electronic Health Records

Francisco J. R. Ruiz
Marie Skłodowska-Curie Fellow
University of Cambridge & Columbia University

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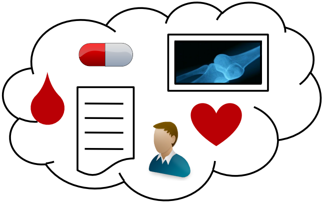
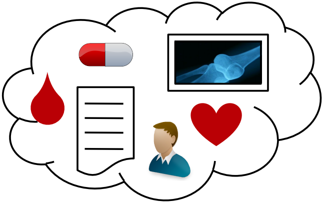
Complex & Unstructured Datasets



Machine learning problems

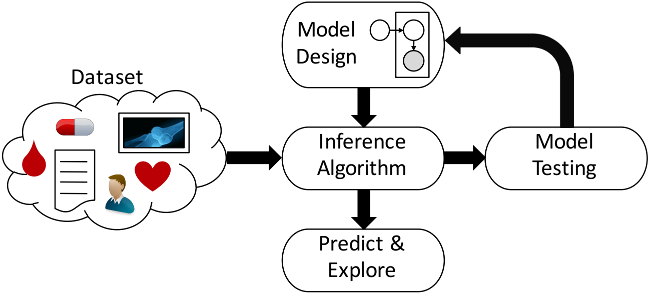
- Large unstructured datasets
- Goal: Make predictions, identify hidden patterns

Probabilistic Machine Learning



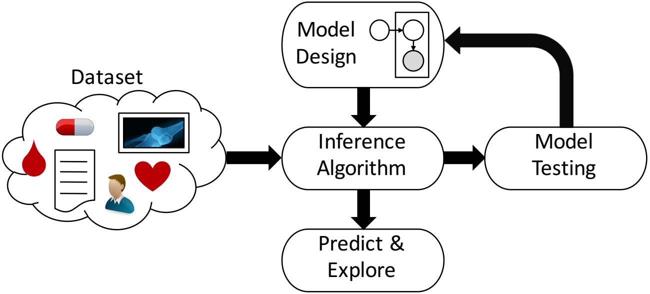
- Connect domain knowledge to data
- Uncertainty quantification
- Scalable computational tools

Probabilistic Machine Learning



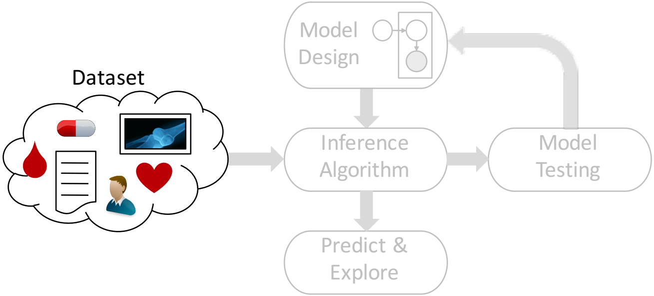
- Posit generative process with hidden and observed variables
- Given the data, reverse the process to infer hidden variables
- Use hidden structure to make predictions, explore the dataset, etc.

Probabilistic Machine Learning



- Incorporate domain knowledge with interpretable components
- Separate assumptions from computation
- Facilitate collaboration with domain experts

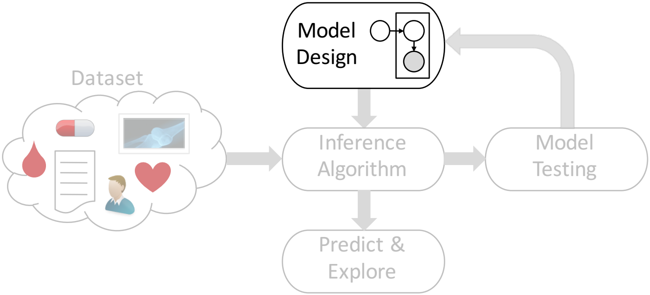
EHR Data is Challenging to Analyze



EHR Data is Challenging to Analyze

- Heterogeneous nature
- Noisy, missing observations
- Longitudinal
- Unobserved variables
- Large-scale datasets
- Observational
- ...

Probabilistic Models

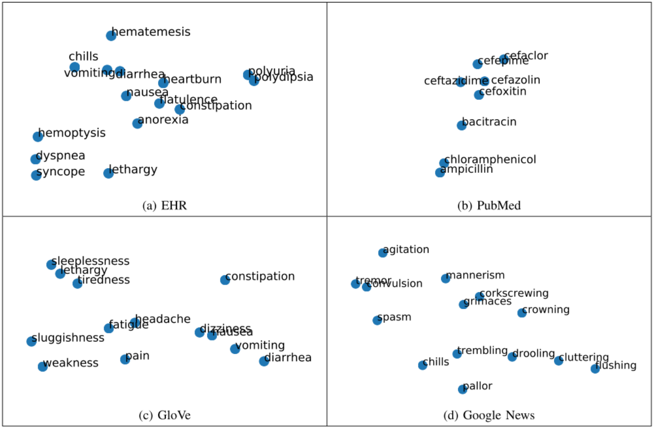


Embedding Representations

- Find latent embedding representations of different data types
  - Medical conditions
  - Neural activity
  - Discrete or continuous data types
- Use the embeddings in a probabilistic model of heterogeneous data

Word Embeddings

Word embeddings find distributed representations of individual words



(Image from Wang et al., 2018)

Word Embeddings

- Word embeddings are a powerful tool for analyzing language
  - Words are placed in a low-dimensional latent space
  - Distances capture semantic similarity

"she has had progressive difficulties with her breathing since she was admitted to hospital for respiratory failure"

$$p(\text{breathing} \mid \text{context})$$

Exponential Family Embeddings

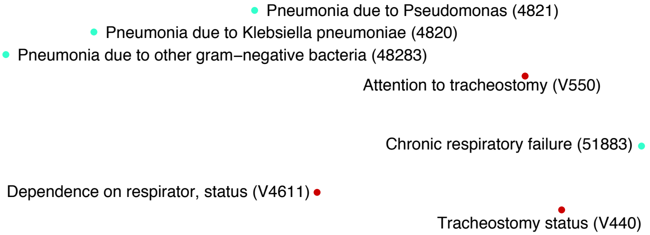
- Can we find distributed features of other types of data?
  - Medical conditions
  - Neural activity
  - Discrete or continuous data types

- **Goals:**
  - Capture *data-to-data* interactions
  - Improve the *predictions* of matrix factorization
  - Obtain *features* that are useful for downstream analyses

[Rudolph+, NeurIPS 2016]

Exponential Family Embeddings

- Main idea: Distill the components of word embeddings
- Applications: Condition embeddings, neuron embeddings, ...
- Tools: Exponential families & Generalised linear models

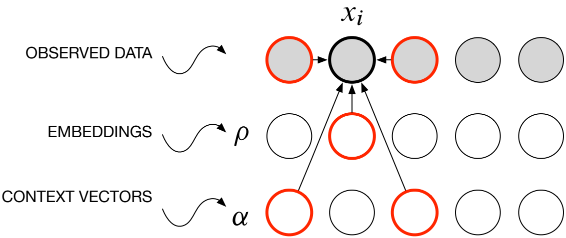


Exponential Family Embeddings

- Observations x_i:

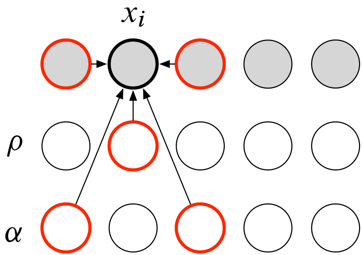
DOMAIN	INDEX	VALUE
Language	position in text i	word indicator
Medical conditions	condition and patient (c, p)	condition present
Neuroscience	neuron and time (n, t)	activity level

Exponential Family Embeddings: Model Description



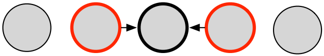
- Two latent vectors per data index (embedding, context)
- Model each data point conditioned on its context
- The latent variables interact in the conditional

Exponential Family Embeddings: Model Description



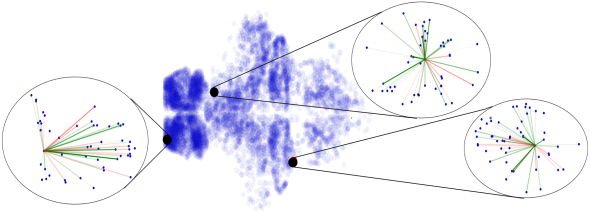
- Three ingredients:
  context, *conditional exponential family*, *embedding structure*

Exponential Family Embeddings: Context



- Each data point i has a *context* $\mathcal{C}_i$, a set of indices
- The conditional of x_i depends on its context $\mathcal{C}_i$

Exponential Family Embeddings: Context



DOMAIN	DATA POINT	CONTEXT
Language	word	surrounding words
Medical conditions	condition presence	other conditions of patient
Neuroscience	neuron activity	surrounding neurons

Exponential Family Embeddings: Exponential Family

- Use exponential families for the conditional of each data point,

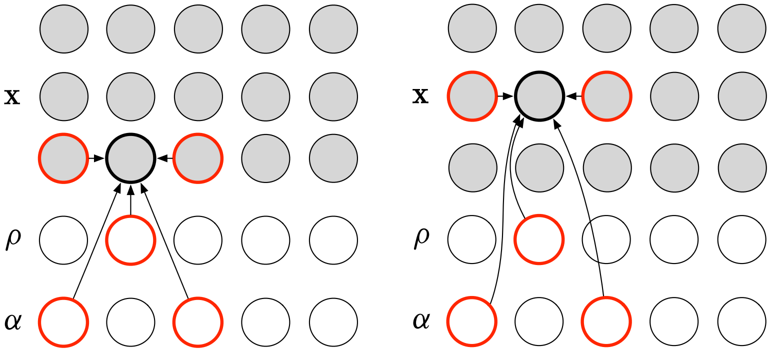
$$p(x_i \,|\, \mathbf{x}_{\mathcal{C}_i}) = \textsc{ExpFam}(\eta_i(\mathbf{x}_{\mathcal{C}_i}), t(x_i))$$

- The natural parameter combines the embedding and context vectors,

$$\eta_i(\mathbf{x}_{\mathcal{C}_i}) = f_i\left(\rho[i]^\top \sum_{j \in \mathcal{C}_i} \alpha[j] x_j\right)$$

  - $f_i(\cdot)$: Link function (identity, log, ...)

Exponential Family Embeddings: Embedding Structure



- The embedding structure determines how parameters are shared
- $\rho[i] = \rho[j]$ for $i = (\text{pneumonia}, p)$ and $j = (\text{pneumonia}, p')$

Exponential Family Embeddings: Objective Function

- Model each datapoint conditioned on its context

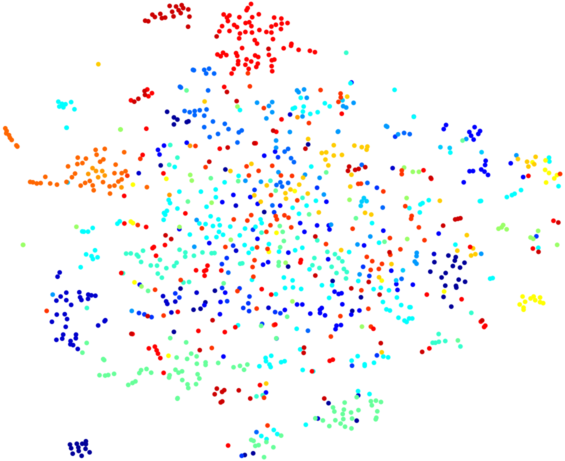
- Combine these terms in a pseudolikelihood

$$\mathcal{L}(\rho, \alpha) = \sum_i \left(\eta_i^\top t(x_i) - a(\eta_i) \right) + \mathcal{L}^{(\mathrm{reg})}$$

- Fit the embedding by maximising $\mathcal{L}(\rho, \alpha)$

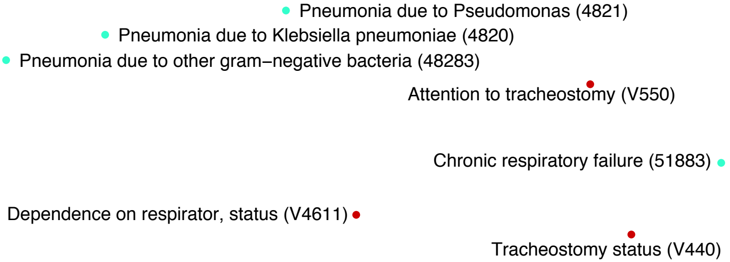
Exponential Family Embeddings: Results

Results on MIMIC-III dataset



Exponential Family Embeddings: Results

Results on MIMIC-III dataset (zoom)



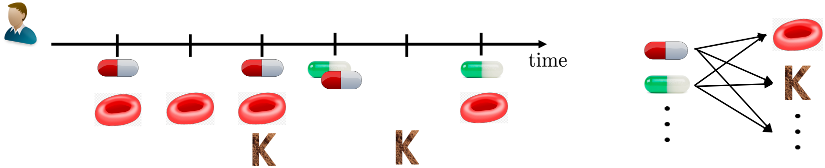
Exponential Family Embeddings: Results and Extensions

- The fitted embeddings are interpretable
- The fitted embeddings have good predictive performance
- Extensions of EFEs:
  - Combine with more complex probabilistic models
  - Structured embeddings
  - Blend with causality ideas

[Liu+, NeurIPS 2017] [Rudolph+, NeurIPS 2017] [Ruiz+, AOAS 2019]

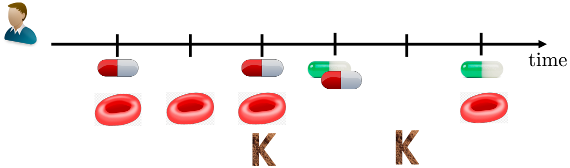
Modelling Heterogeneous Longitudinal Data

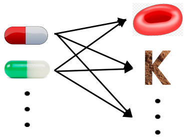
- Data: Events in time (drugs, labs, conditions)
- 250K patients from New York Presbyterian Hospital



Modelling Heterogeneous Longitudinal Data

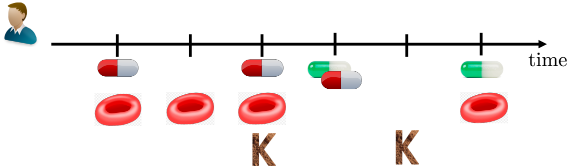
- Effect of drugs on lab tests

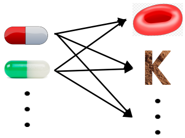




Modelling Heterogeneous Longitudinal Data

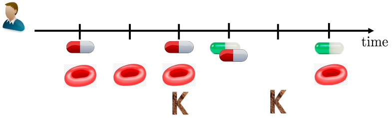
- Learn from measurement values but also from their presence

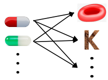


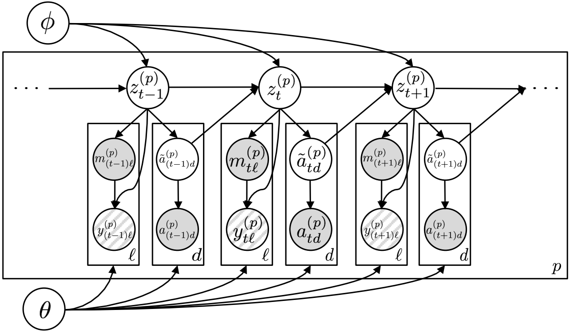


Modelling Heterogeneous Longitudinal Data

- A first model: Linear dynamical system

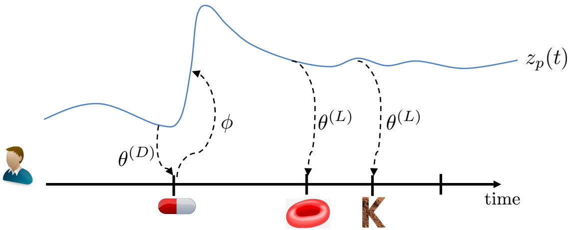






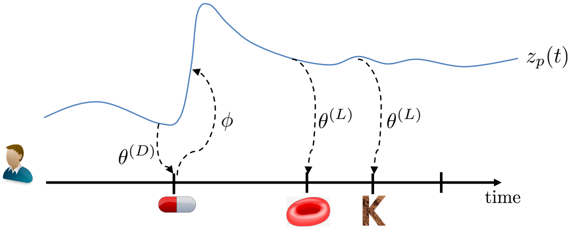
Modelling Heterogeneous Longitudinal Data

- Continuous extension
- Extract information from time stamps and event types
- Model: temporal point processes with per-patient latent rate

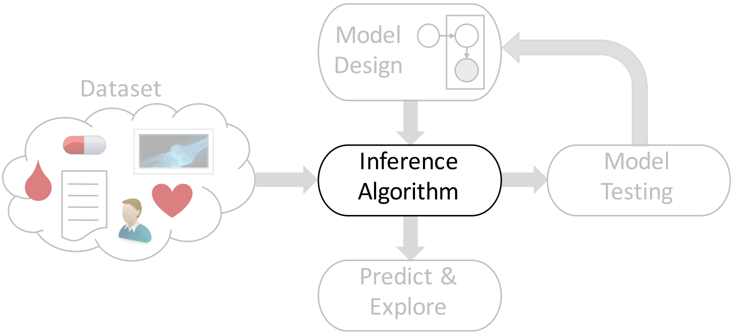


Modelling Heterogeneous Longitudinal Data

- Use embedding representations to form the likelihood
- Embeddings are latent variables in the model



Scalable Inference



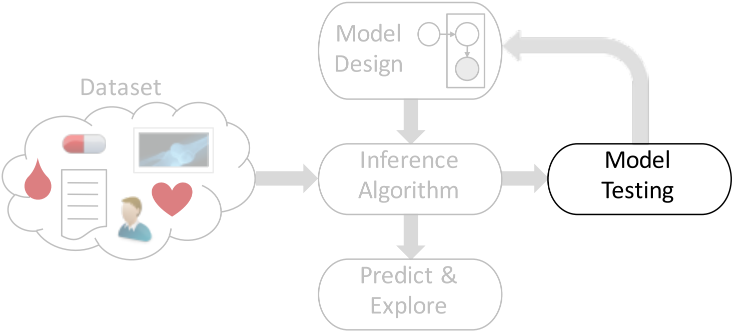
Scalable Inference

- Approximate the posterior of the latent variables given data
- Variational inference
- Scalable to:
  - Complex, non-conjugate models
  - Large numbers of observations
  - High-dimensional latent variables

Contributions on Variational Inference

- Scale-up inference for categorical observations with many outcomes
  [Ruiz+, ICML 2018]
- Reduce variance of gradient estimators
  [Ruiz+, NeurIPS 2016] [Naesseth+, AISTATS 2017]
- More expressive variational families
  [Titsias+, AISTATS 2019] [Ruiz+, ICML 2019]

Model Testing



Model Testing

- Context: Probabilistic modelling for causal inference
- Problems:
  - Causal inference requires many assumptions
  - Standard Bayesian testing tools are not applicable
- Contribution: A method to check the validity of the assumptions

[Tran+, preprint 2017]

Conclusions

- Probabilistic modelling is a powerful tool for analyzing EHR data
- Contributions on
  - **Modelling:** Exponential family embeddings, point process latent health model, . . .
  - **Variational inference:** Scale up categoricals, reduce gradient variance, more expressive variational families
  - **Testing:** Bayesian causal model testing

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