Mortality assessment in ICU with multivariate physiological time-series

2/21/12

Danning He, DHSI, JHSOM
Mentor: Jim Fackler, Harold Lehmann

Outline

- Project summary
- Background
- Technical Approach
- Deliverables
- Timeline
- Management Plan
- Reading List

Project Summary

- The ICU is a complex, expensive and data-intensive environment. Tools that automatically interpret patterns in the data are crucial for clinical decision-making.
- The goal is to develop mortality models that predicts in-hospital death based on multiple clinical temporal data during the first two days of an ICU stay.

Supervised learning: Classical scoring system

- APACHE: Acute Physiology and Chronic Health Evaluation
- SAPS: Simplified Acute Physiology Score
- MPM: Mortality Probability Models (MPM0, MPM24)
- SOFA: Sequential Organ Failure Assessment score
- Many others.

Table 1. Comparison of general outcome prediction models

Characteristics	APACHE [3]	SAPS [10]	APACHE II [4]	MPM[a] [14]	APACHE III [5]	SAPS II [11]	MPM II[b] [15]	SAPS 3 [12]	APACHE IV [8]	MPM III [17]
Year	1981	1984	1985	1985	1991	1993	1993	2005	2006	2007
Countries	1	1	1	1	1	12	12	35	1	1
ICUs	2	8	13	1	40	137	140	303	104	135
Patients	705	679	5,815	2,783	17,440	12,997	19,124	16,784	110,558	124,855
Selection of variables and their weights	Panel of experts	Panel of experts	Panel of experts	Multiple logistic regression	Multiple logistic regression	Multiple logistic regression	Multiple logistic regression	Multiple logistic regression	Multiple logistic regression	Multiple logistic regression
Variables										
Age	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Origin	No	No	No	No	Yes	No	No	Yes	Yes	No
Surgical status	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Chronic health status										
Physiology										
Acute diagno										
Number of variab										
Score										
Mortality predicti										

[a]These models are
(MPM$_0$ II). [c]MPM$_{24}$ I
Score; MPM, Morta

Table 2. Comparison of three organ dysfunction scores

Characteristics	LODS [29]	MODS [30]	SOFA [31]
Year of publication	1996	1995	1996
Selection of variables and their weights	Multiple logistic regression	Literature review and logistic regression	Panel of experts
Variables used to assess organ dysfunction			
Neurologic	Glasgow Coma Scale	Glasgow Coma Scale	Glasgow Coma Scale
Cardiovascular	Heart rate, systolic blood pressure	Pressure-adjusted heart rate	Mean arterial blood pressure, vasopressor use
Renal	Serum urea or urea nitrogen, creatinine, urine output	Serum creatinine	Serum creatinine, urine output
Respiratory	PaO_2/FiO_2 ratio, mechanical ventilation	PaO_2/FiO_2 ratio	PaO_2/FiO_2 ratio, mechanical ventilation
Hematologic	White blood cell count, platelet count	Platelet count	Platelet count
Hepatic	Serum bilirubin, prothrombin time	Serum bilirubin	Serum bilirubin

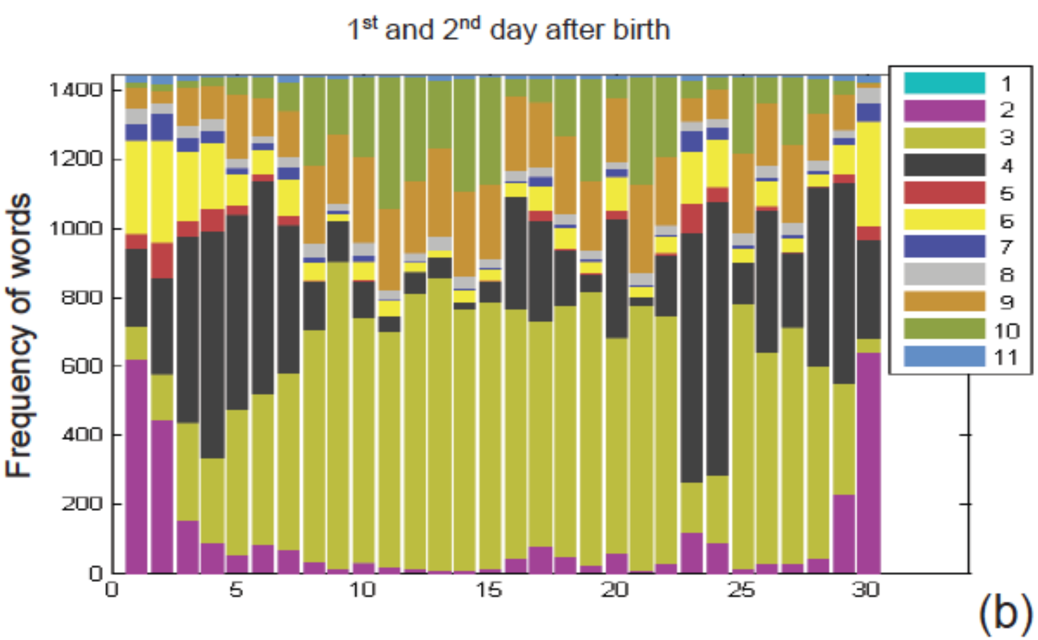
LODS, Logistic Organ Dysfunction Score; MODS, Multiple Organ Dysfunction Score; SOFA, Sequential Organ Dysfunction Score.

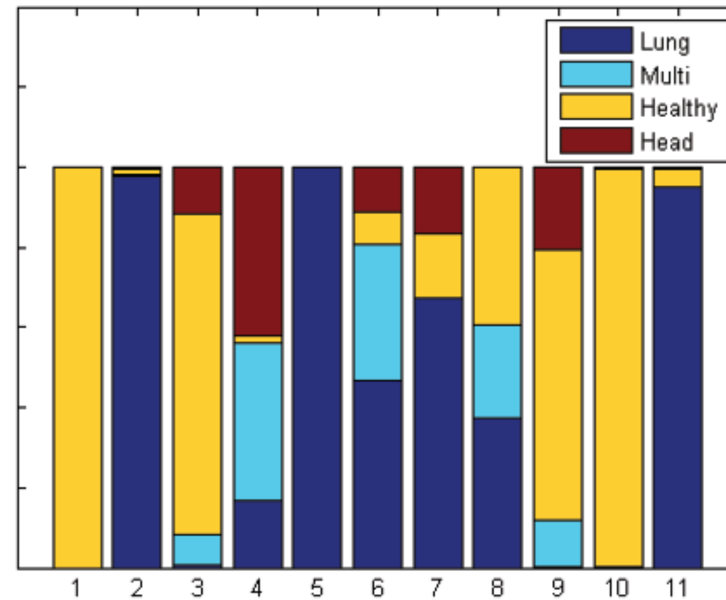
Vincent JL and Moreno R. (2010). "Clinical review: scoring systems in the critically ill." Crit Care. **14**(2): 207.

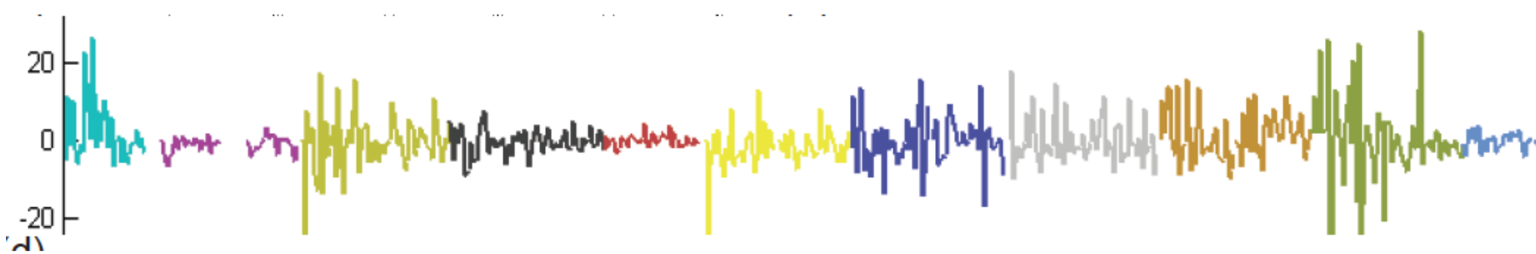
Unsupervised learning: State-space

- Real-world processes produce series of measureable observations as a function of underlying hidden states.
- Similar to clinical diagnosis, which is inferred from several observations with significant degree of uncertainty, generation of multivariate physiologic profiles by latent disease status or signatures can help reveal the manifestation of disease.

Latent states in univariate and continuous clinical time-series







Saria S, Koller D, et al. (2010). "Learning individual and population level traits from Clinical Temporal data." <u>Neural Information Processing Systems.</u>

Interest in Translational Medicine

- BMC Genomics. 2011 Dec 2;12:592.

Identification of dysfunctional modules and disease genes in congenital heart disease by a network-based approach.

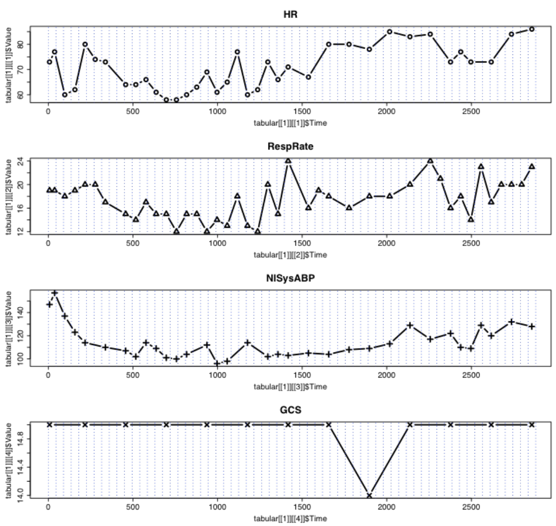
Danning He, Zhi-Ping Liu, Luonan Chen[1]

- JMCB. Accepted

Coexpression network analysis in chronic hepatitis B and C hepatic lesion reveals distinct patterns of disease progression to hepatocellular carcinoma

Danning He[1,2,†], Zhi-Ping Liu[1,†,*], Masao Honda[3], Shuichi Kaneko[3] and Luonan Chen[1,*]

Technical Approach: General framework



…
37 time-series

Group into ‘topic’ →

Cardiovascular
Neurology
Respiratory
Hematologic
Other ‘topic’

→ Acuity score of topics over time → Logistic regression

Technical approach: Logistic regression model

- For two-class classification, the probability of class 'mortality' (C1) given original variables (X) can be written as a logistic sigmoid acting on the linear combination of the feature vector $\phi = \phi(X)$ so that
- $$p(C_1 \mid X) = \sigma\left(-\mathbf{w}^T \phi\right) = \frac{1}{1+\exp\left(-\mathbf{w}^T \phi\right)}$$
- where $\phi(\cdot)$ is the basis function that transforms original variables into feature vectors.

Technical approach: multivariate, discrete, irregular measurement

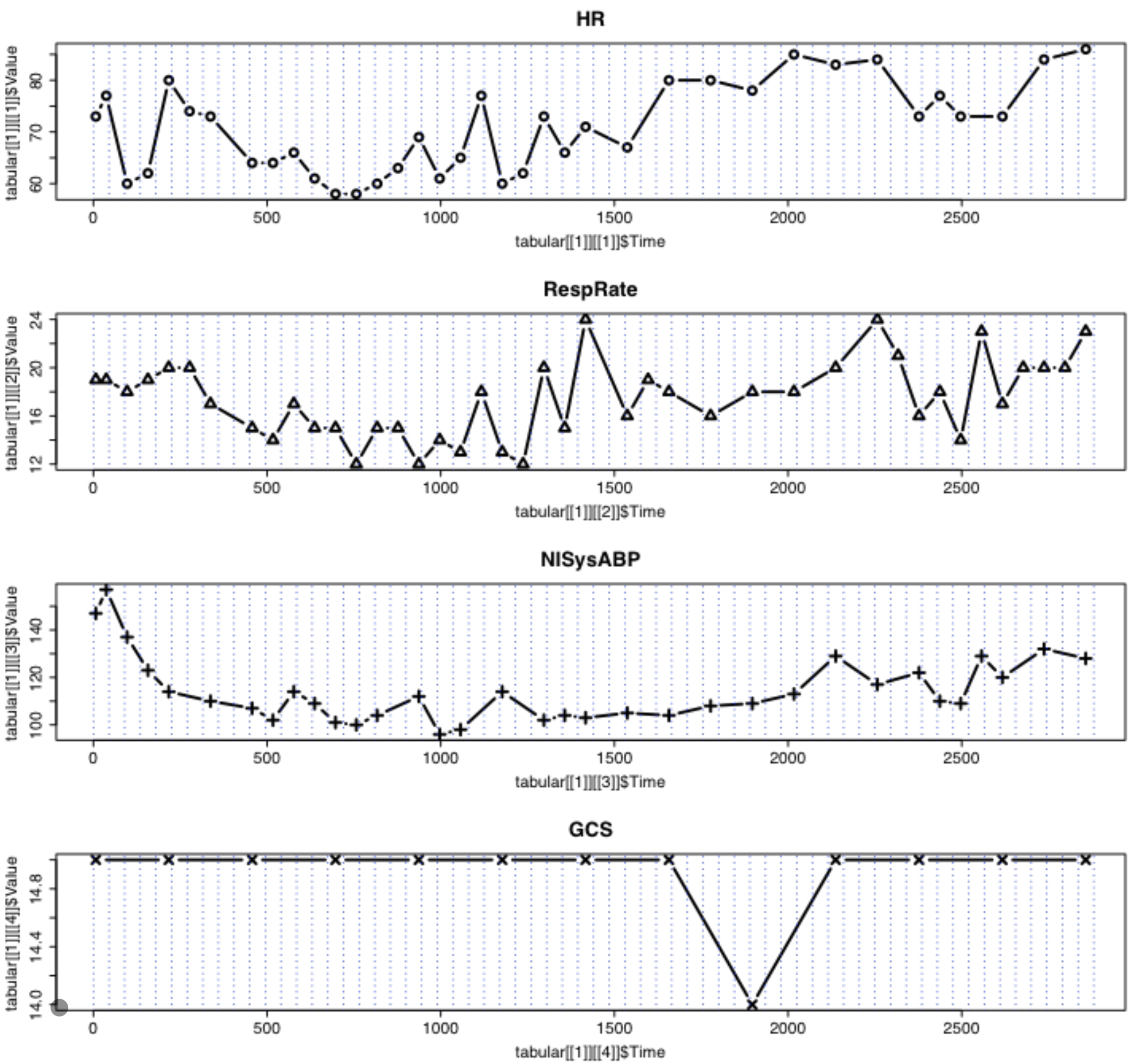
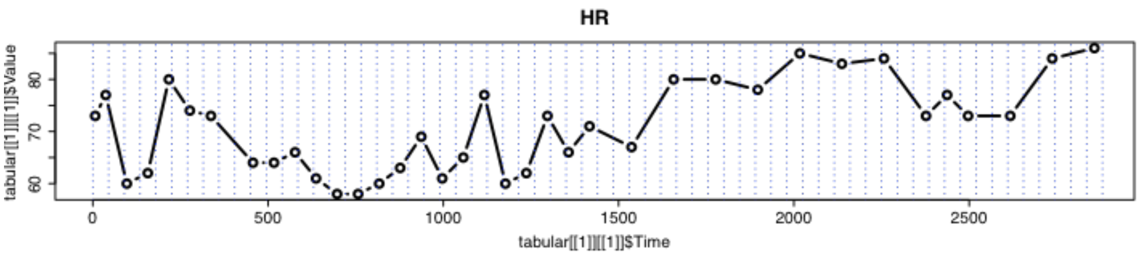


Figure 1. y-axis: value, x-axis: time

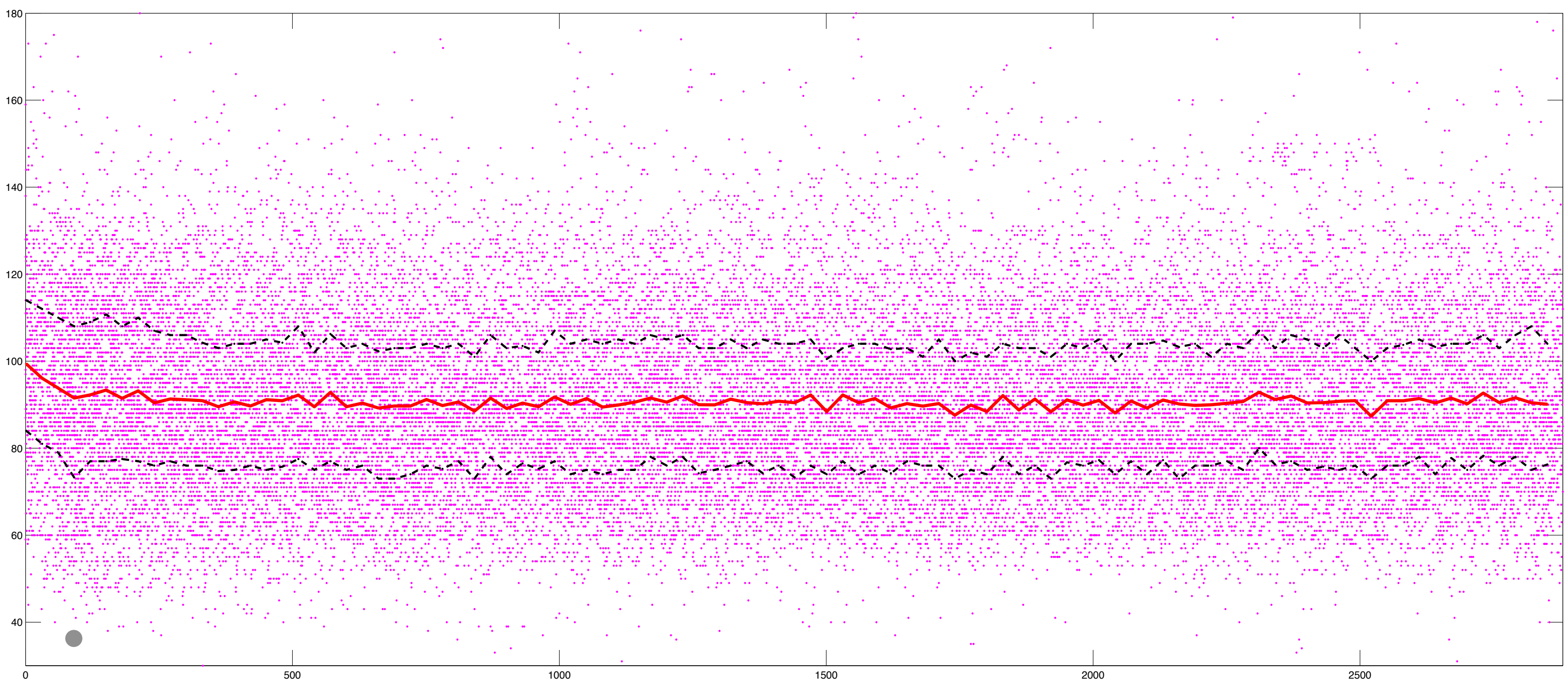
- *HR* [Heart rate (bpm)]
- *RespRate* [Respiration rate (bpm)]
- *NISysABP* [Non-invasive systolic arterial blood pressure (mmHg)]
- *GCS* [Glasgow Coma Score (3-15)]

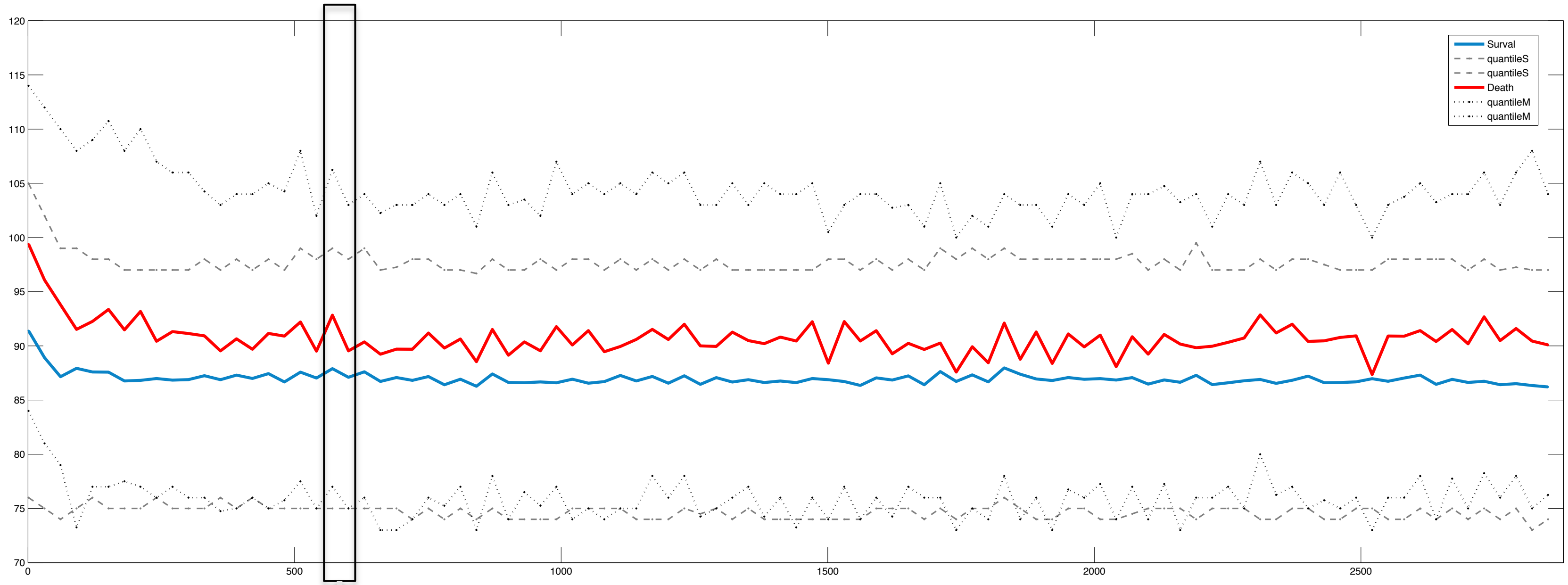
Technical approach: population characteristics



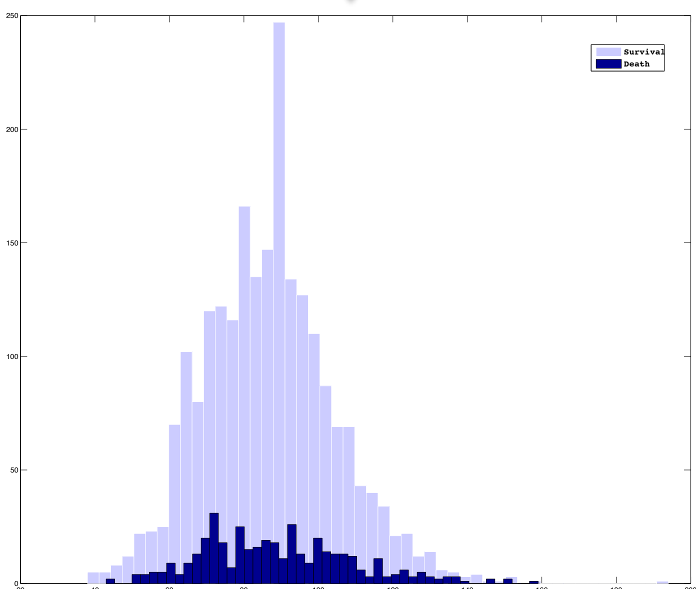
Heart Rate: One individual

Heart Rate: Population

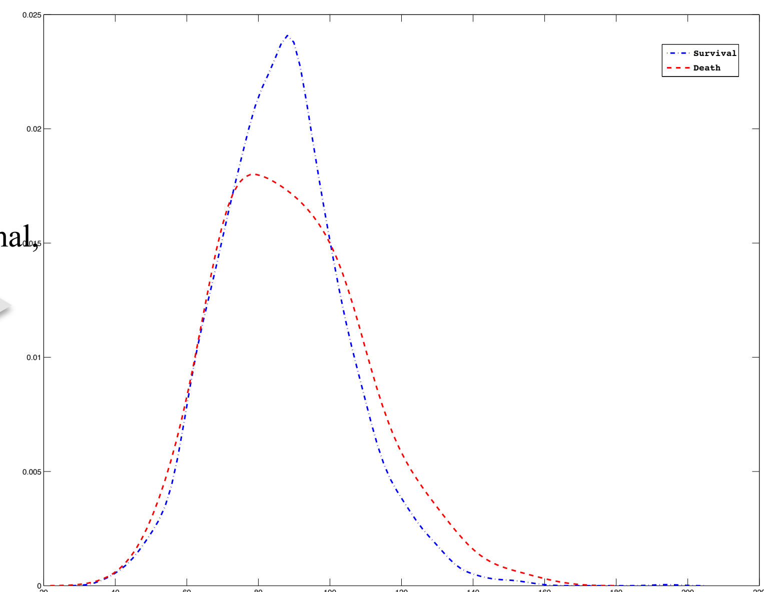




For each risk factor: A time slice

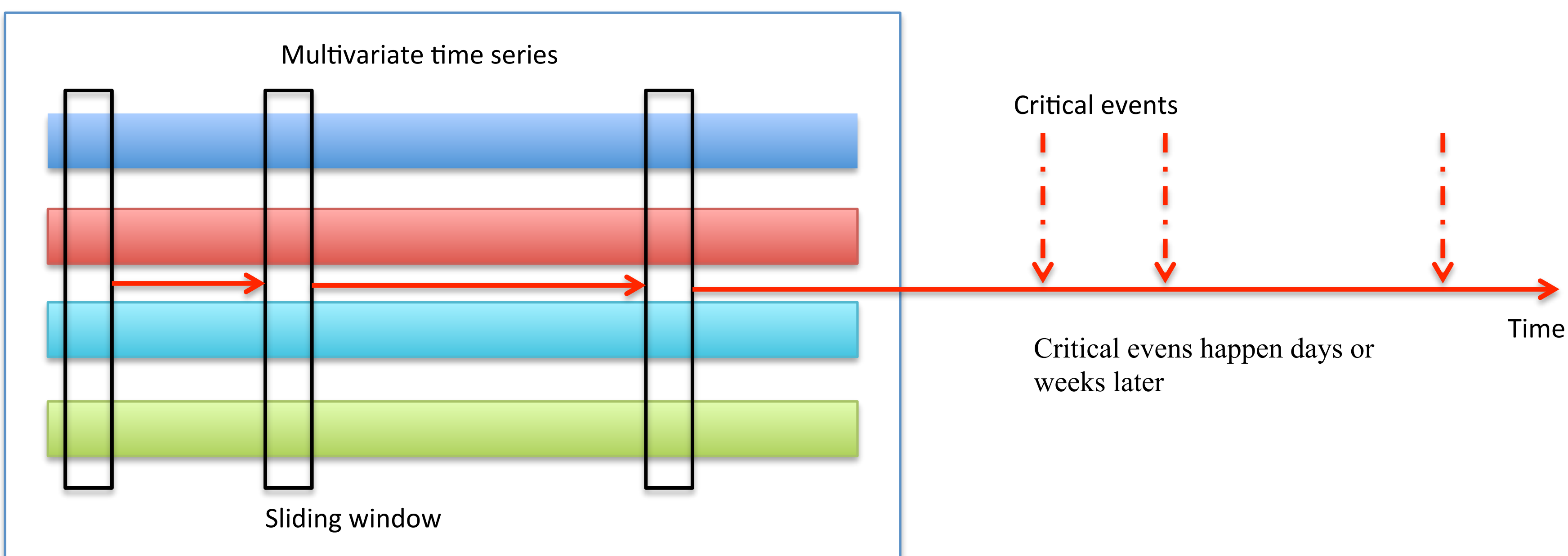


fit parametric distribution: normal, exponential…??

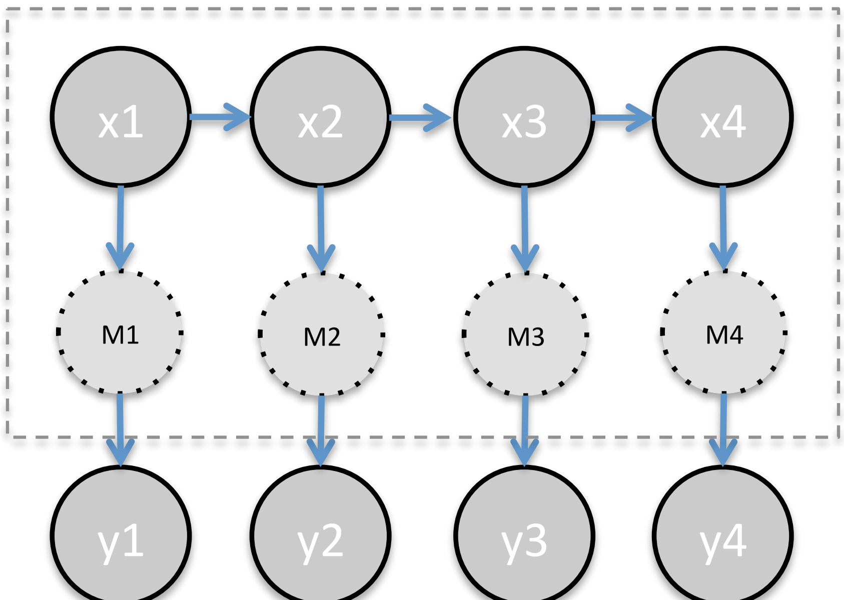


Technical Approach: feature as log odds ratio of risk factors

$$\phi_{it} = \log\left(\frac{p\left(v_{it} \mid C_1\right)}{p\left(v_{it} \mid C_2\right)}\right)$$



Technical Approach: Feature as hidden states?



Multivariate observations

Deliverables

- **Minimum**

-- Logistic regression with log odds ratios as risk features

-- Performance evaluation: ROC, AUC

- **Expected**

-- Minimum deliverables

-- Incorporating waiting time until the critical events

-- Try features constructed from standard HMM, Kalman Filter

- **Maximum**

-- Expected deliverables

-- Optimize features to achieve better classification performance

Management Plan

- Regular weekly meeting/consult with Dr. Fackler or Dr. Lehmann
- Frequent consult with related experts when necessary
- Update wiki pages regularly at weekends, documentation of the work done in the past week and the work that will be done in the following week
- Report progress regularly to Dr. Fackler and Dr. Lehmann

Timeline

Timeline		week 1	week 2	week 3	week 4	week 5	week 6	week 7	week 8	week 9	week 10	week 11	week 12
Milestone 1	reading list												
	project plan												
	preprocessing data												
Milestone 2 (Minimum)	Features as log odds ratio												
	Logistic regression												
	AUC and ROC												
Milestone 3 (Expected)	try HMM												
	try Kalman Filter												
	Optimization												
Milestone 4	Model comparison												
	Project report												

Reading List

- 1. Saria S, Koller D, Penn AA. (2010) Learning individual and population level traits from Clinical Temporal data. Neural Information Processing Systems.
- 2. Imhoff M, Kuhls S. (2006) Alarm algorithms in critical care monitoring. Anesth Analg 102: 1525-1537.
- 3. Zimmerman JE, Kramer AA, McNair DS, Malila FM. (2006) Acute Physiology and Chronic Health Evaluation (APACHE) IV: hospital mortality assessment for today's critically ill patients. Crit Care Med 34: 1297-1310.
- 4. Ferreira FL, Bota DP, Bross A, Mélot C, Vincent JL. (2001) Serial Evaluation of the SOFA Score to Predict Outcome in Critically Ill Patients. JAMA 286: 1754-1758.
- 5. Silva A, Cortez P, Santos MF, Gomes L, Neves J. (2006) Mortality assessment in intensive care units via adverse events using artificial neural networks. Artif Intell Med 36: 223-234.
- 6. Hug CW, Szolovits P. (2009) ICU Acuity: Real-time Models versus Daily Models. AMIA Annu Symp Proc: 260-264.
- 7. Saria S, Rajani AK, Gould J, Koller D, Penn AA. (2010) Integration of Early Physiological Responses Predicts Later Illness Severity in Preterm Infants. Sci Transl Med 2: 48ra65.

Thank you for your attention.