

# Learning DBNs & Non-Homogeneous DBNs from Incomplete data in Intensive Care

Federico Pirola, Fabio Stella, Marco Grzegorczyk, Anna Lavizzari



$$\frac{P(B|A) \times P(A)}{P(B)}$$

# Sections

## PRELIMINARIES

- Dynamic Bayesian Networks: definition and application domains
- Bayesian Statistics and Montecarlo methods

## LEARNING DBNs FROM INCOMPLETE DATA

- Issues in Observational Settings
- LUME-DBN: A full Bayesian method for learning DBNs from Incomplete Data
- Applications in Intensive Care
  - Physionet Case Study
  - Bronchopulmonary Dysplasia Case Study

## NON STATIONARY TEMPORAL MODELS

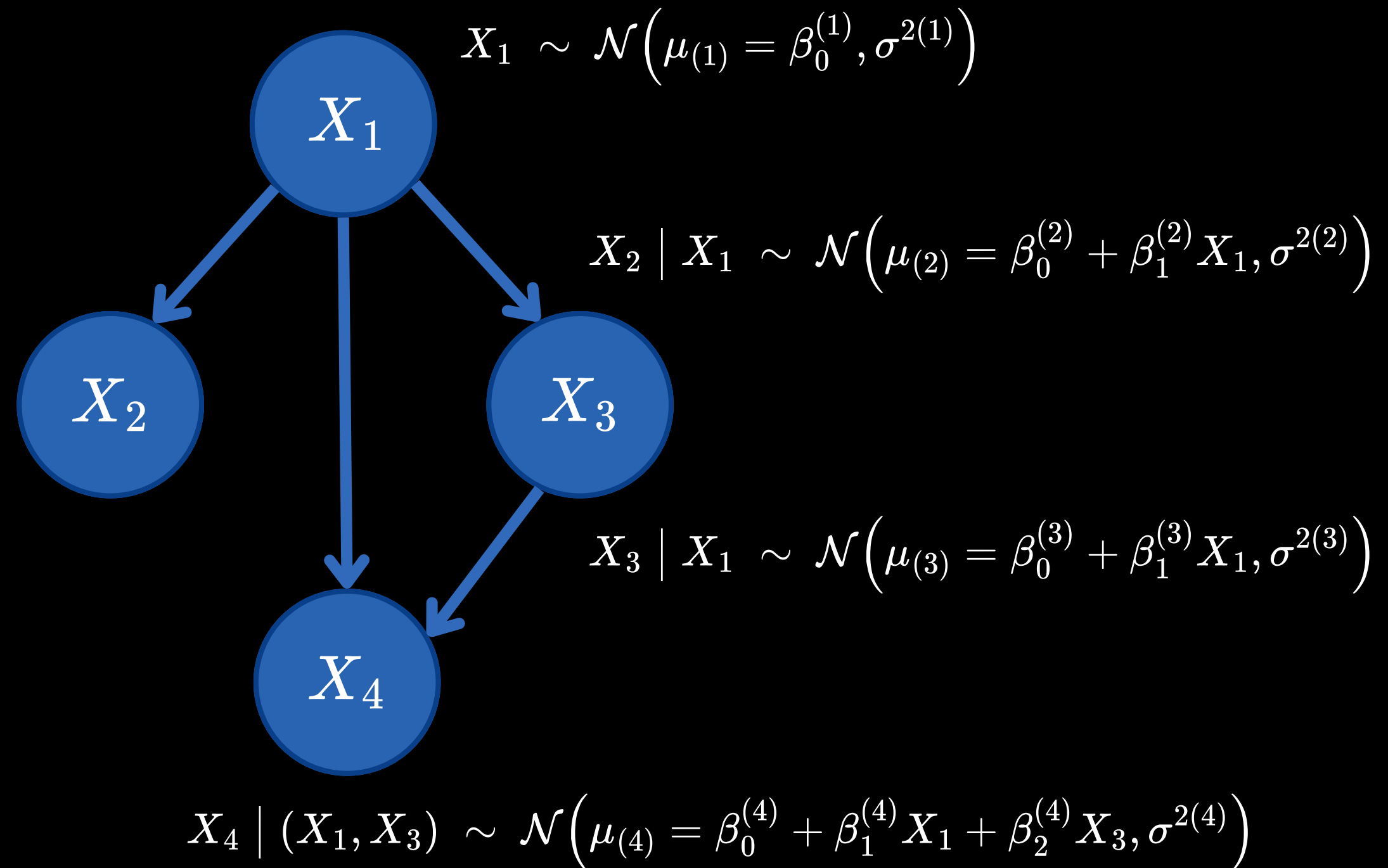
- Non-stationary and Non-Homogeneous DBNs
- LUME-NH: A full Bayesian method for learning NH-DBNs from Incomplete Data

# Dynamic Bayesian Networks

# Probabilistic Graphical Models

Highly interpretable Machine Learning models widely employed in biomedical domains

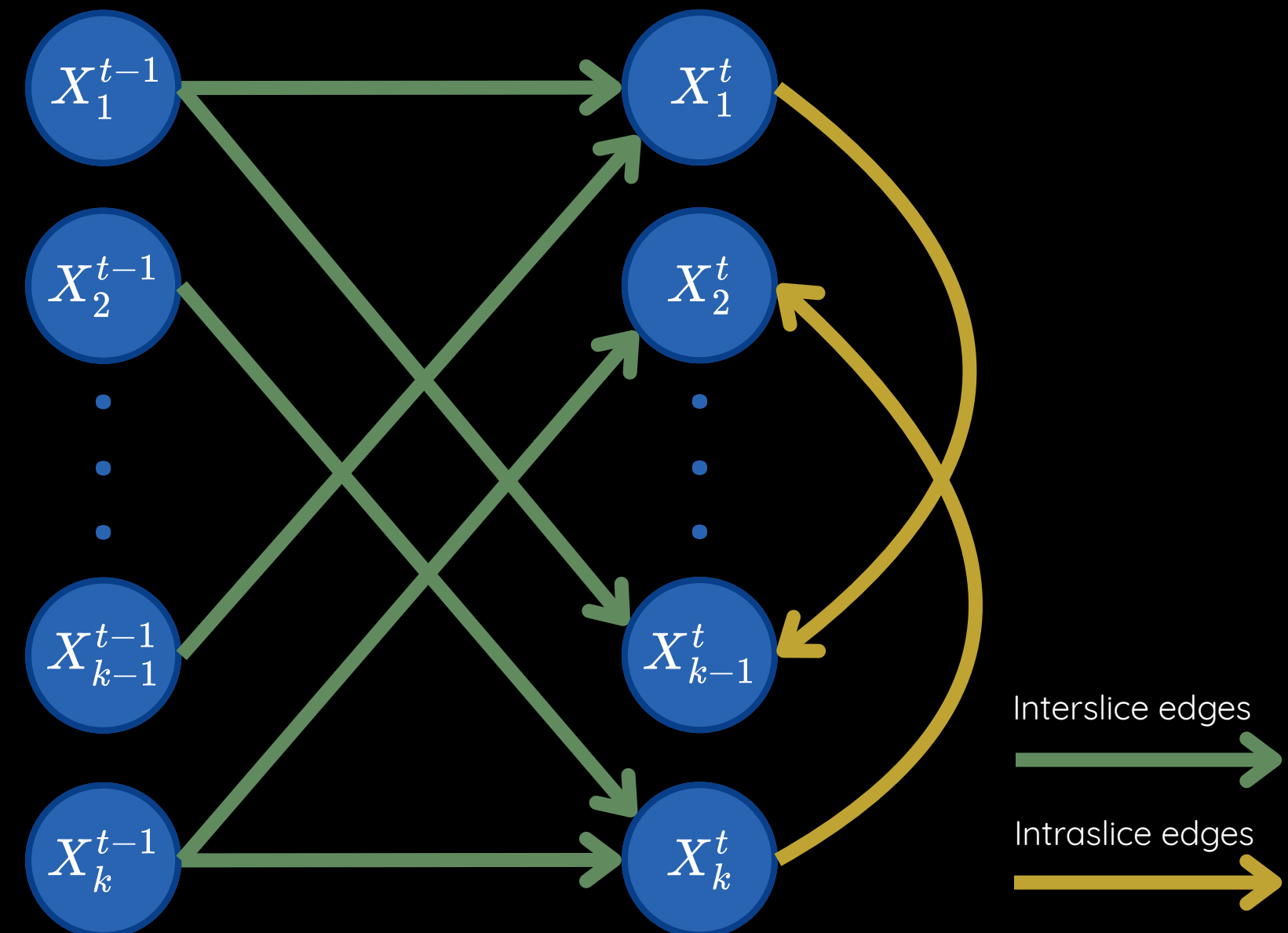
- **MODELS:** modeling the dependencies between multiple random variables
- **GRAPHICAL:** characterised by a graphical representation encoding conditional dependencies and independencies
- **PROBABILISTIC:** described by a set of conditional probability distributions





# Dynamic Bayesian Networks

- **Dynamic Bayesian networks** (DBNs) **model** the **temporal evolution** of **multivariate continuous time series** factorizing the joint distribution of all variables across time into a **product of conditional distributions for each node**
- **Dynamic Bayesian networks** (DBNs) are described as a set of:
  - A **structure**, represented by a **Transition Network** encoding the relationship between the **nodes at time t-1** and the **nodes at time t**
  - A **set of parameters** encoding the **linear relationships** between a variable and its parent set



# Application domains and the context of Intensive Care Data

- DBNs are effective across **various domains** including **biology**, **healthcare domain** and **environmental data**. They have been used to learn gene regulatory networks, predict disease progression, and spatio-temporal environmental modeling.
- In the context of **Intensive Care Units (ICUs)** they show their value in **integrating heterogeneous ICU time-series data** and delivering **interpretable decision support** in the setting of **severe patients care**.



# **Bayesian Statistics & Markov Chain Monte Carlo**

# Frequentist Statistics vs Bayesian Statistics

***Frequentist statistics** treats parameters as fixed but **unknown constants**. It evaluates the likelihood of observed data looking for the value of the **unknown parameters** which **maximize the likelihood**.*

$$\hat{\theta} = \max_{\theta} p(X|\theta)$$

**Frequentist**: “What parameter value best explains the observed data?”

# Frequentist Statistics vs Bayesian Statistics

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Frequentist: “What parameter value best explains the observed data?”

**Bayesian statistics** views **parameters as random variables with probability distributions**. **Prior beliefs** about these parameters are **updated with observed data** to produce **posterior distributions**. It directly **model uncertainty over the parameters** through their distributions.

$$p(\theta|X) = \frac{p(\theta) \cdot p(X|\theta)}{p(X)}$$

Bayesian: “Given the data, what is our updated belief over the parameters probability distribution?”

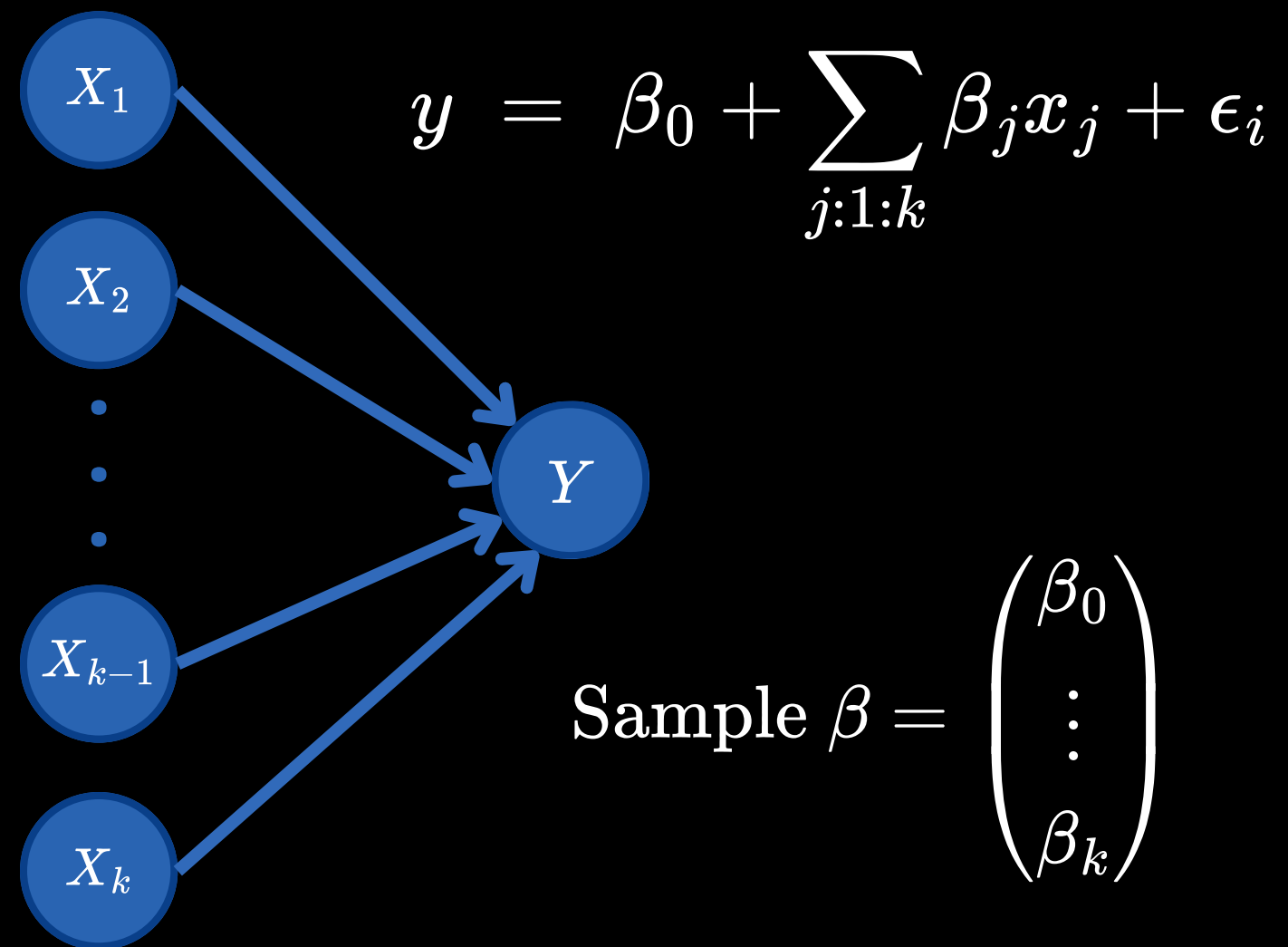
# Markov Chain Monte Carlo (MCMC) Simulations in Bayesian Statistics

Bayesian inference strongly relies on MCMC simulations to approximate posterior expectations when the required integrals cannot be evaluated in closed form.

# Markov Chain Monte Carlo (MCMC) Simulations in Bayesian Statistics

## Standard MCMC Setting

Conditional to the **known model** (structure) the **unknown parameters** are iteratively sampled

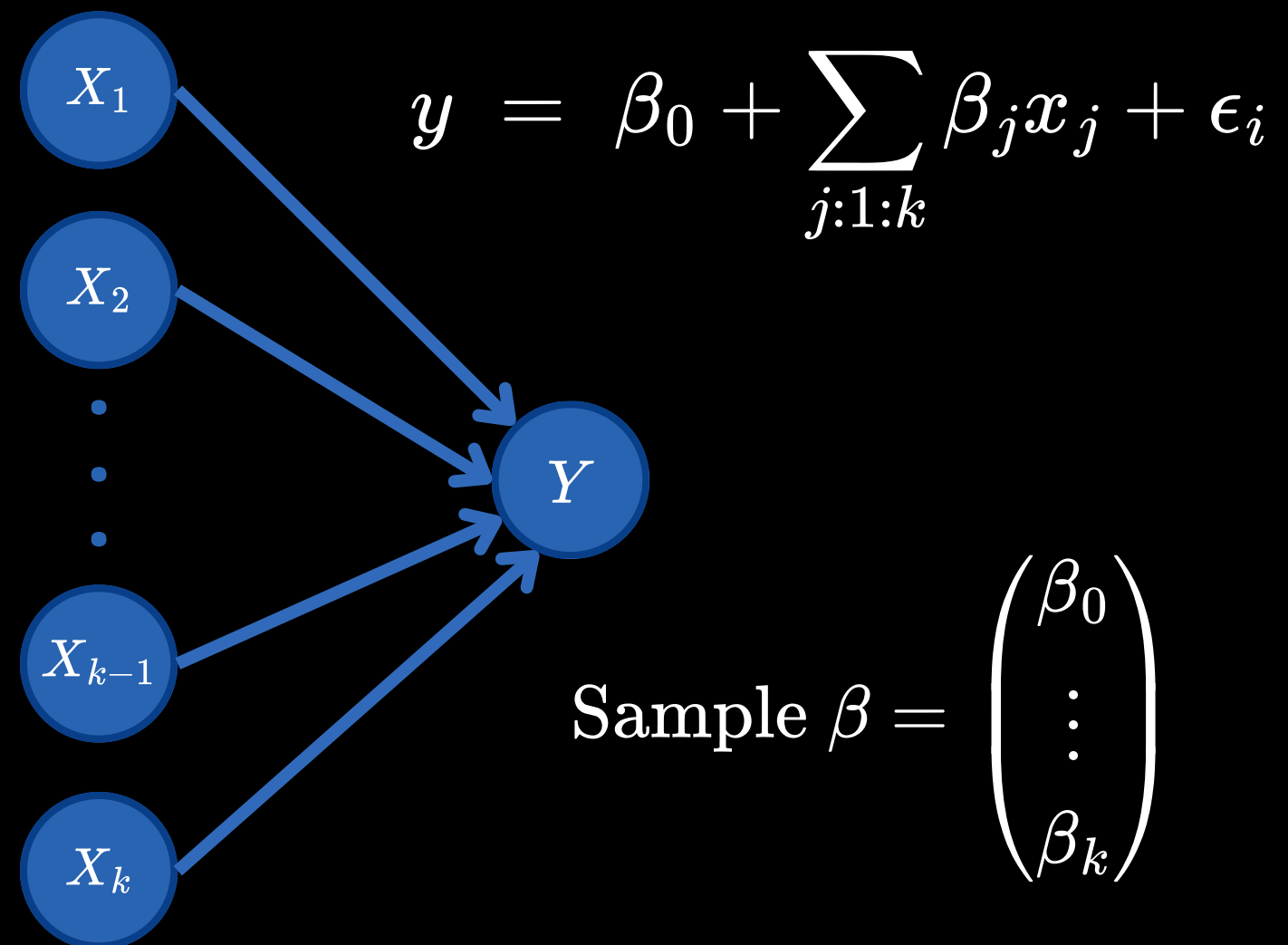


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# Markov Chain Monte Carlo (MCMC) Simulations in Bayesian Statistics

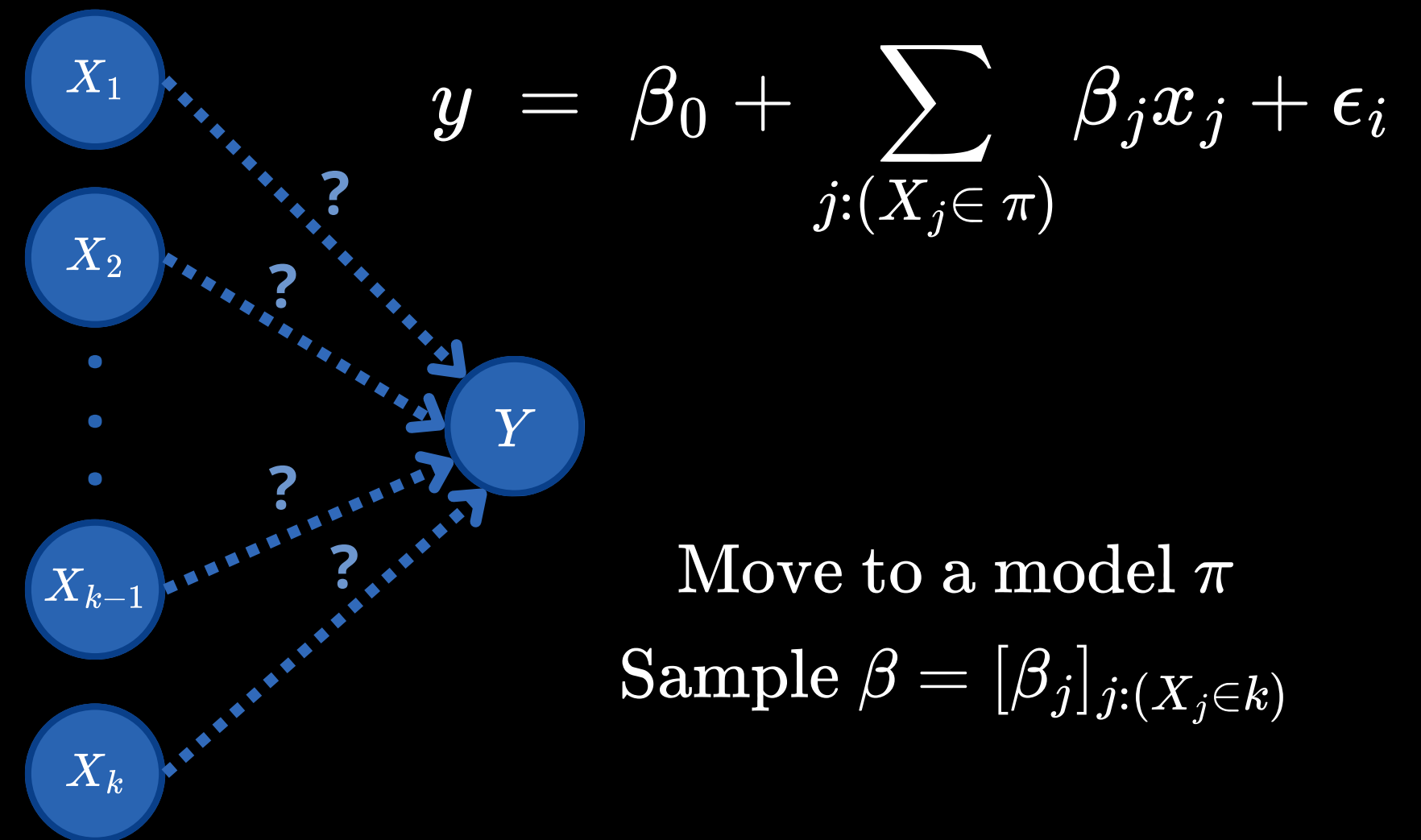
## Standard MCMC Setting

Conditional to the **known model** (structure) the **unknown parameters** are iteratively sampled



## RJMCMC Setting

The **unknown parameters** are sampled jumping between different **unknown models**



Bayesian inference strongly relies on MCMC simulations to approximate posterior expectations when the required integrals cannot be evaluated in closed form.



# Metropolis-Hastings & Gibbs Sampling

**Metropolis-Hastings** (MH) is an MCMC algorithm that constructs a Markov chain by **proposing candidate values, sampled from a proposal distribution** (PD).

1. Initialization of the chain:  $\theta_0$

2. Proposal of a new value sampled from the PD:  $\theta_\star \sim q(\theta_\star | \theta_{t-1})$

3. Compute the Acceptance probability:  $\alpha = \min \left( 1, \frac{p(\theta_\star | \cdot) q(\theta_{t-1} | \theta^\star)}{p(\theta_{t-1} | \cdot) q(\theta_\star | \theta_{t-1})} \right)$

4. Accept the proposed value with  $\alpha > p \sim U(0, 1)$  otherwise keep the previous value  $\theta_{t-1}$

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**Gibbs sampling** (GS) is a **special case of Metropolis-Hastings** where the **PD is the full conditional distribution** (FCD), namely the distribution of the parameter given the current model and data.

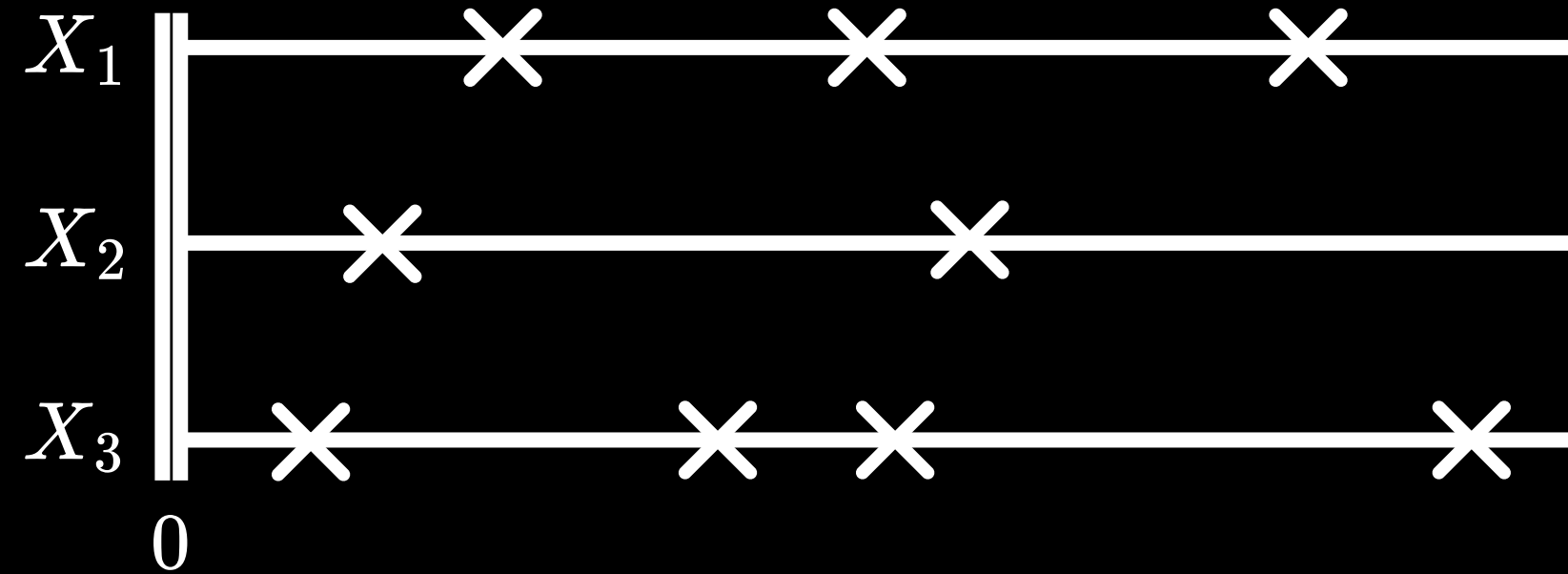
In GS the acceptance probability  $\alpha = \min \left( 1, \frac{p(\theta_\star | \cdot) q(\theta_{t-1} | \theta_\star)}{p(\theta_{t-1} | \cdot) q(\theta_\star | \theta_{t-1})} = \frac{p(\theta_\star | \cdot) p(\theta_{t-1} | \cdot)}{p(\theta_{t-1} | \cdot) p(\theta_\star | \cdot)} \right) = 1$

However **sampling exactly from the FCD is generally intractable** except for conjugate priors frameworks.

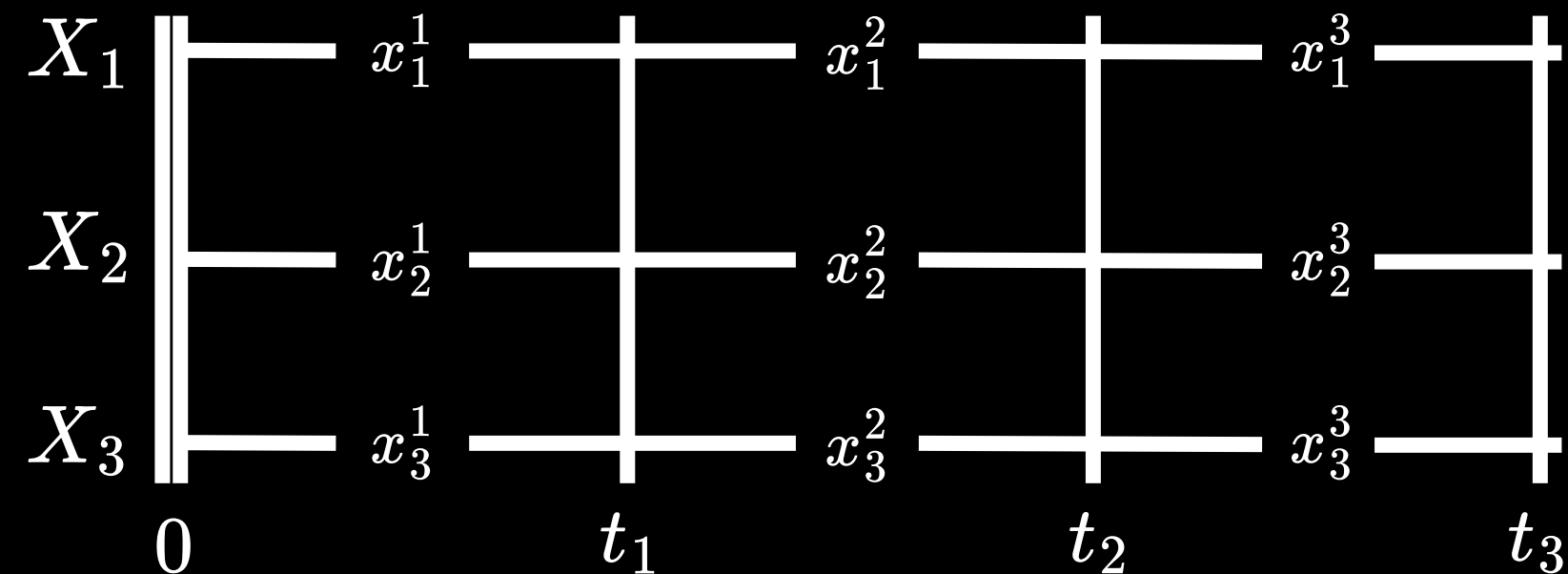
# Issues in Observational Settings

DBNs in Observational Settings

OBSERVATIONAL DATA SCENARIO

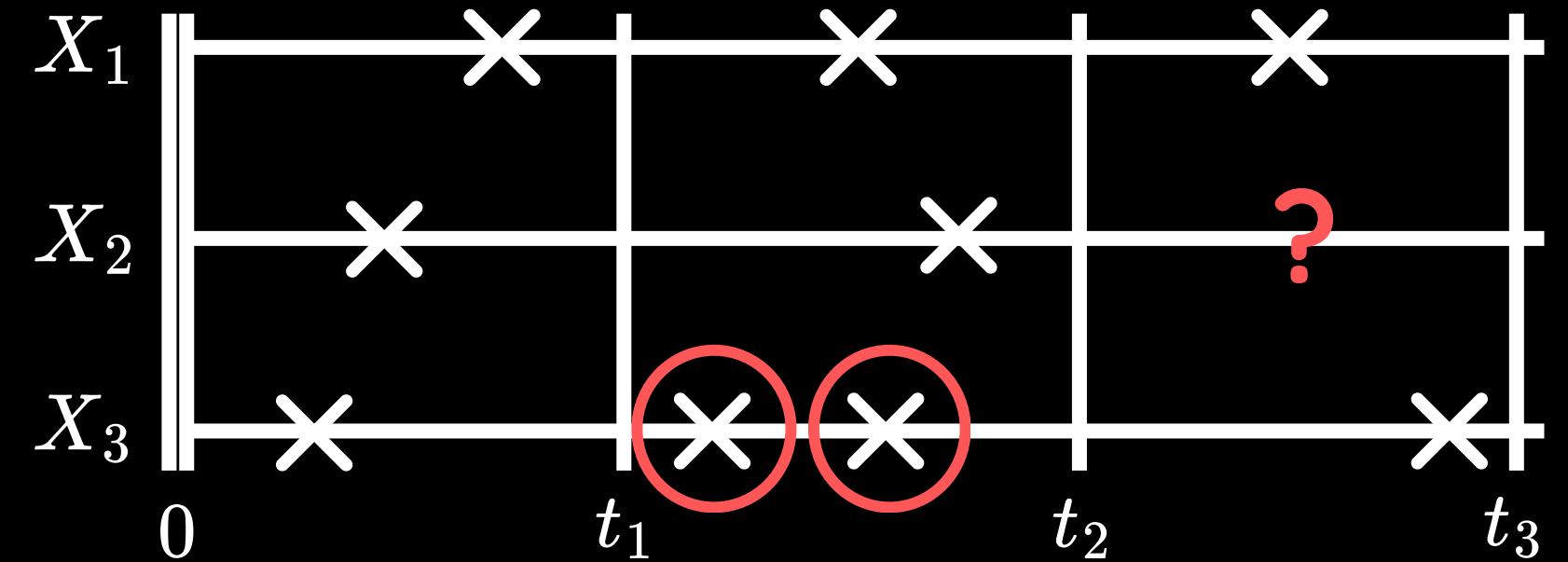


INPUT DATA REQUIRED IN DBNs



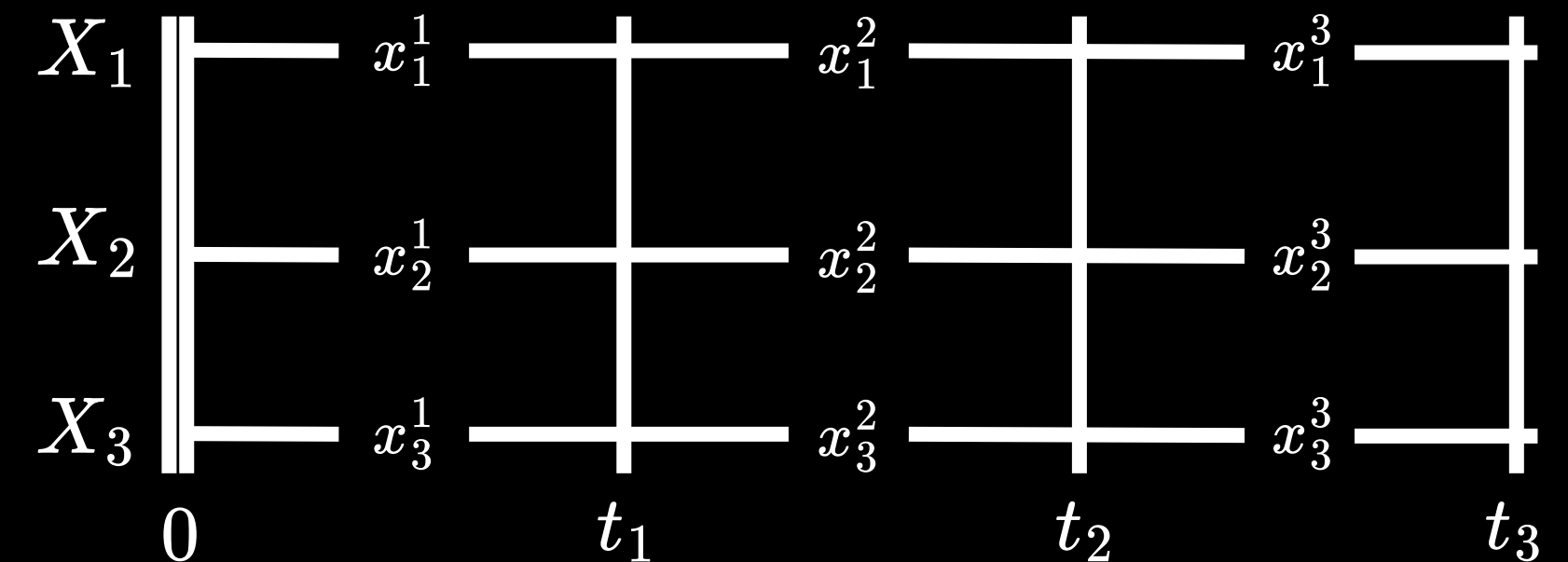
# DBNs in Observational Settings

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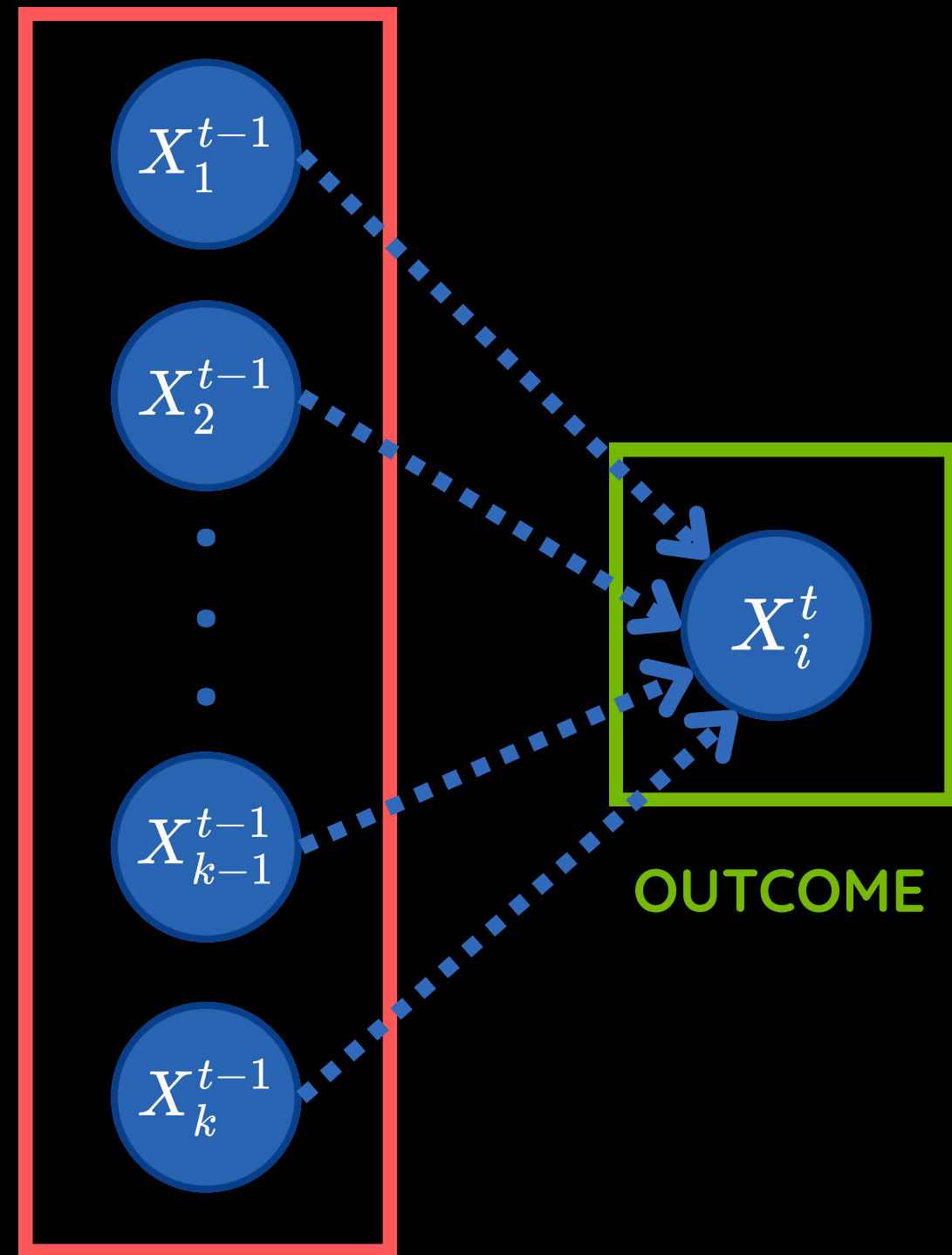


<< How can we manage observations over continuous time in DBN learning? >>

INPUT DATA REQUIRED IN DBNs



# Dynamic Bayesian Networks as a set of Linear Regressions



$$x_i^t = \beta_0^{(i)} + \sum_{j: (X_j^{t-1} \in \pi_{(i)})} \beta_j^{(i)} x_j^{t-1} + \epsilon_i^t$$
$$(t = 1, \dots, T)$$

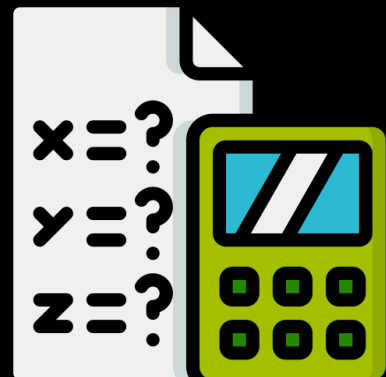
NO ACYCLICITY CONSTRAINT IS  
NEEDED AS IN STATIC BNS !

# Managing Missing Values in DBNs

ICU data are characterized by **irregular sampling frequencies** and incorrect detection, leading to **Incomplete Data**

## STANDARD IMPUTATION

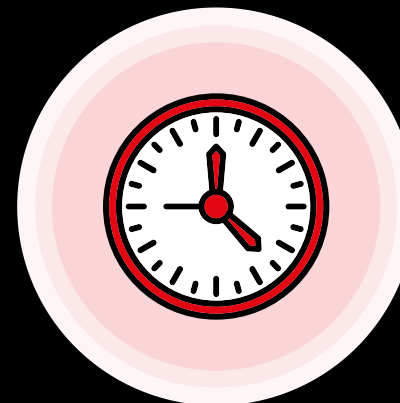
i.e. MICE Imputation



- ⊕ REALLY FAST
- ⊖ MODEL AGNOSTIC
- ⊖ POINT ESTIMATES

## FREQUENTIST APPROACHES

i.e. Structural EM



- ⊕ ITERATIVE UPDATES
- ⊕ MODEL-DEPENDENT
- ⊖ LOCAL MINIMA RISK
- ⊖ NOT DBN-SPECIFIC

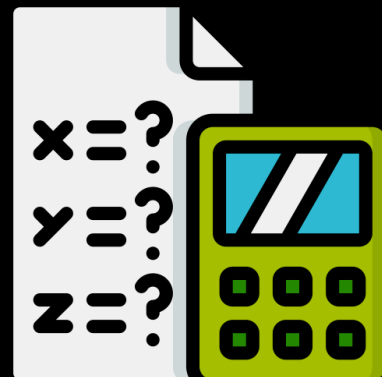
*STATE OF THE ART*

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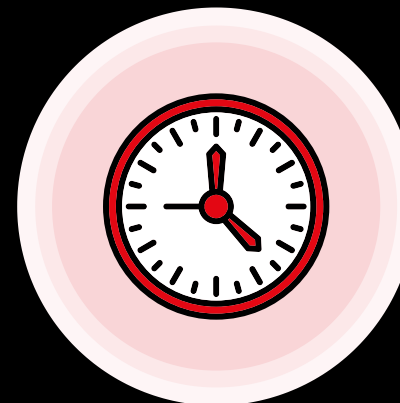


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***STATE OF THE ART***

## FREQUENTIST APPROACHES

i.e. Structural EM



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- ⊕ MODEL-DEPENDENT
- ⊖ LOCAL MINIMA RISK
- ⊖ NOT DBN-SPECIFIC

## FULL BAYESIAN METHOD

LUME-DBN



- ⊕ MODEL UNCERTAINTY
- ⊕ AVOID LOCAL MINIMA
- ⊕ DBN-SPECIFIC
- ⊕ CONVERGENCE TO THE RIGHT SOLUTION

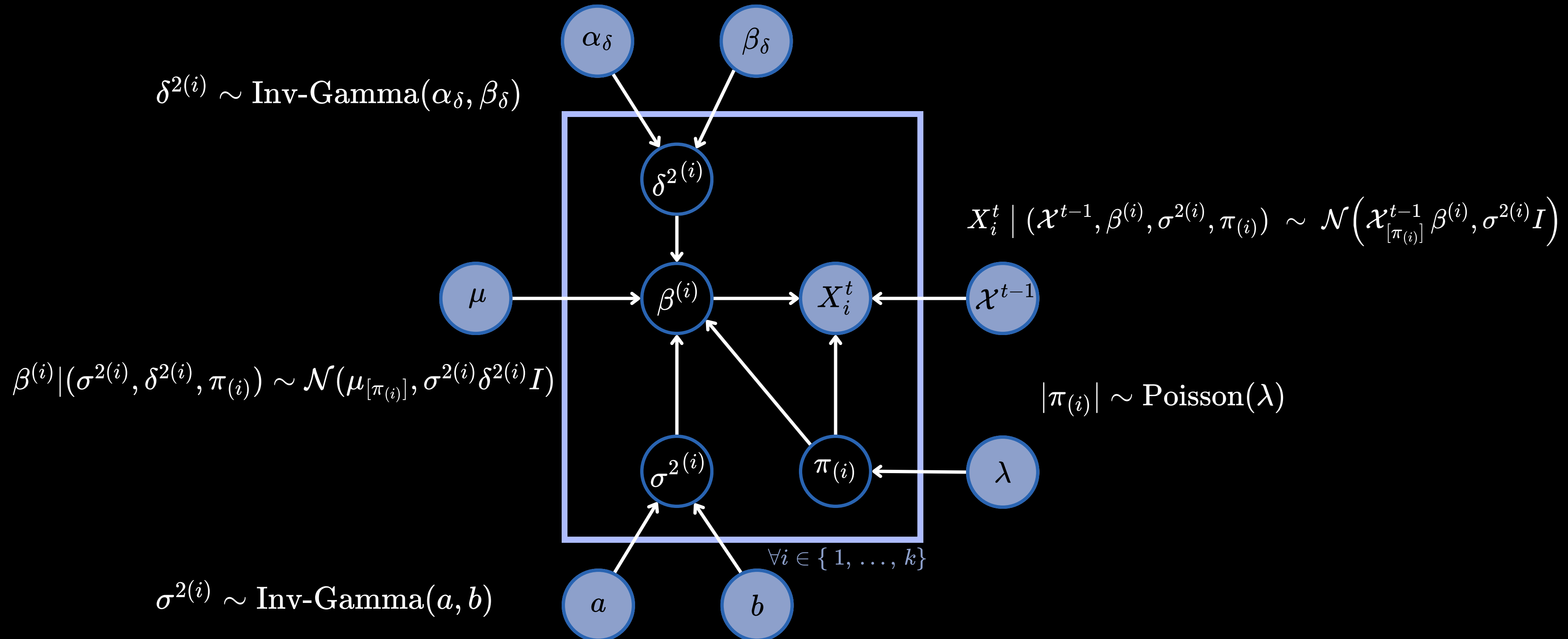
***OUR PROPOSAL***



# Learning DBNs from Incomplete Data

# A Bayesian Formulation of Dynamic Bayesian Networks

Since intra-slice edges are ruled out, the task of learning a DBN could be segmented in k distinct BLR learning tasks



# Learning DBNs from Incomplete Data

Learning the DBN is then the task of **learning** the **structure** and the set of **parameters** that describe the **relationships between temporal nodes** in the Transition Network. To **learn a DBN from data**, we consider a group of **N samples partially observed at T+1 equally spaced time points**, where each sample is described by a **set of k variables**.

INITIAL DATASET

Sample	Time	X1	X2
s1	0.3	?	3
s1	1.2	2	5
s1	1.8	4	7
s2	0.9	9	?
s2	1.5	4	1

TEMPORALLY DISCRETIZED DATA

Sample	Time	X1	X2
s1	0	2	3
s1	1	3	6
s2	0	9	?
s2	1	1	4

LAGGED DATA

Sample	Time	X1 (t-1)	X1 (t)	X2 (t-1)	X2 (t)
s1	1	2	3	3	6
s2	1	9	1	?	4

# LUME-DBN Algorithm

Latent Uncertainty Modeling via MCMC Estimation in DBNs (**LUME-DBN**) is the first **full bayesian method** for **learning DBNs** from **Incomplete data**. Employing our Gibbs sampling imputation step, LUME-DBN is characterized by an iterative procedure following **three main steps**:

For each  
outcome  
variable

$\beta$   
 $\sigma$   $\delta$

PARAMETERS UPDATES: COLLAPSED GIBBS SAMPLING STEP



STRUCTURAL UPDATES: METROPOLIS-HASTING STEP



MISSING VALUES IMPUTATION: GIBBS SAMPLING STEP

For each  
sample and  
time frame

# Structure and Parameter Updates

Conditional  
on the  
current  
structure  
and missing  
values

Sampling  $\sigma^2, \beta, \delta^2$  from their Full Conditional Distributions (FCDs)

$$\left\{ \begin{array}{l} \sigma^2 \sim \text{Inv-GAM} \left( \alpha_\sigma + \frac{NT}{2}, \beta_\sigma + \frac{1}{2} (Y - X_{[\pi]} \mu_{[\pi]})^\top (I + \sigma^2 X_{[\pi]} X_{[\pi]}^\top)^{-1} (Y - X_{[\pi]} \mu_{[\pi]}) \right) \\ \beta \sim \mathcal{N} \left( (\sigma^{-2} I + X_{[\pi]}^\top X_{[\pi]})^{-1} (\sigma^{-2} \mu_{[\pi]} + X_{[\pi]}^\top Y), \sigma^2 (\sigma^{-2} I + X_{[\pi]}^\top X_{[\pi]})^{-1} \right), \\ \delta^2 \sim \text{Inv-GAM} \left( a + \frac{|\pi| + 1}{2}, b + \frac{1}{2} \sigma^{-2} (\beta - \mu_{[\pi]})^\top (\beta - \mu_{[\pi]}) \right) \end{array} \right.$$

# Structure and Parameter Updates

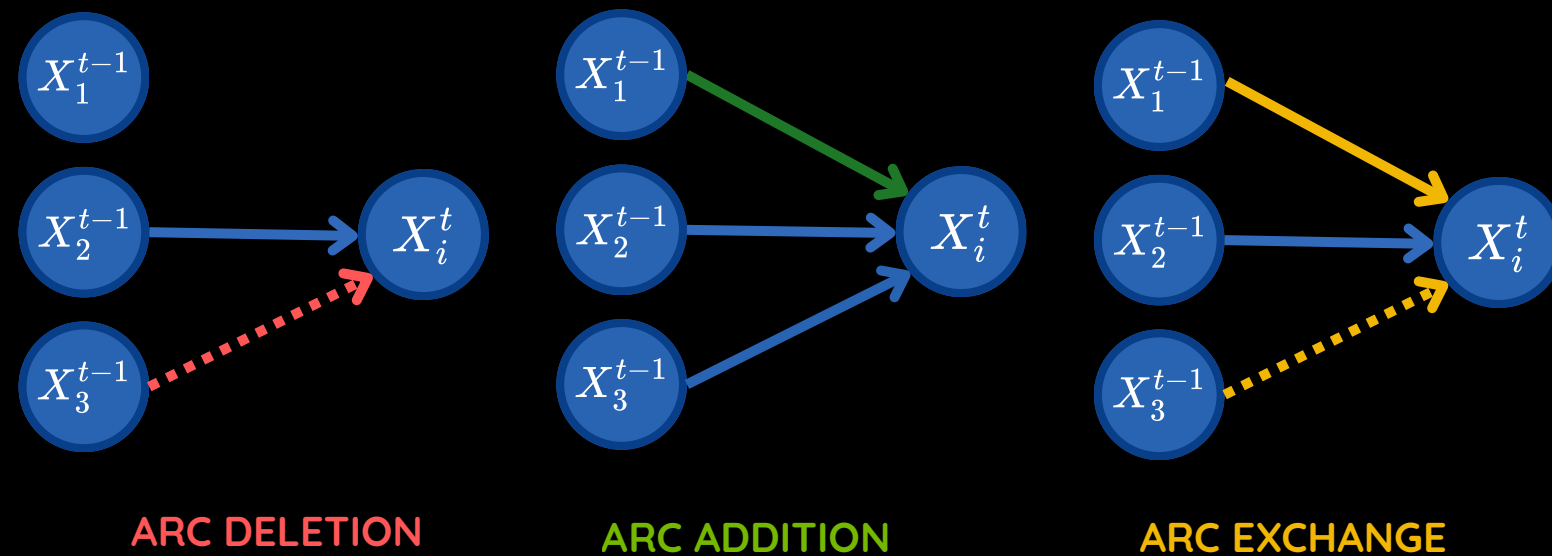
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Conditional  
on the  
imputed  
missing  
values

Sampling a Move and Propose a new Structure



Structural Update Probability of Acceptance

$$A(\pi \rightarrow \pi_\star) = \min \left\{ 1, \frac{p(Y | \pi_\star, \delta^2)}{p(Y | \pi, \delta^2)} \cdot \frac{p(\pi_\star)}{p(\pi)} \cdot HR \right\}$$

Acceptance for  $A > p \sim U(0, 1)$

# Missing Values Update - Gibbs Sampling Step

Compute Missing Values Posterior Parameters

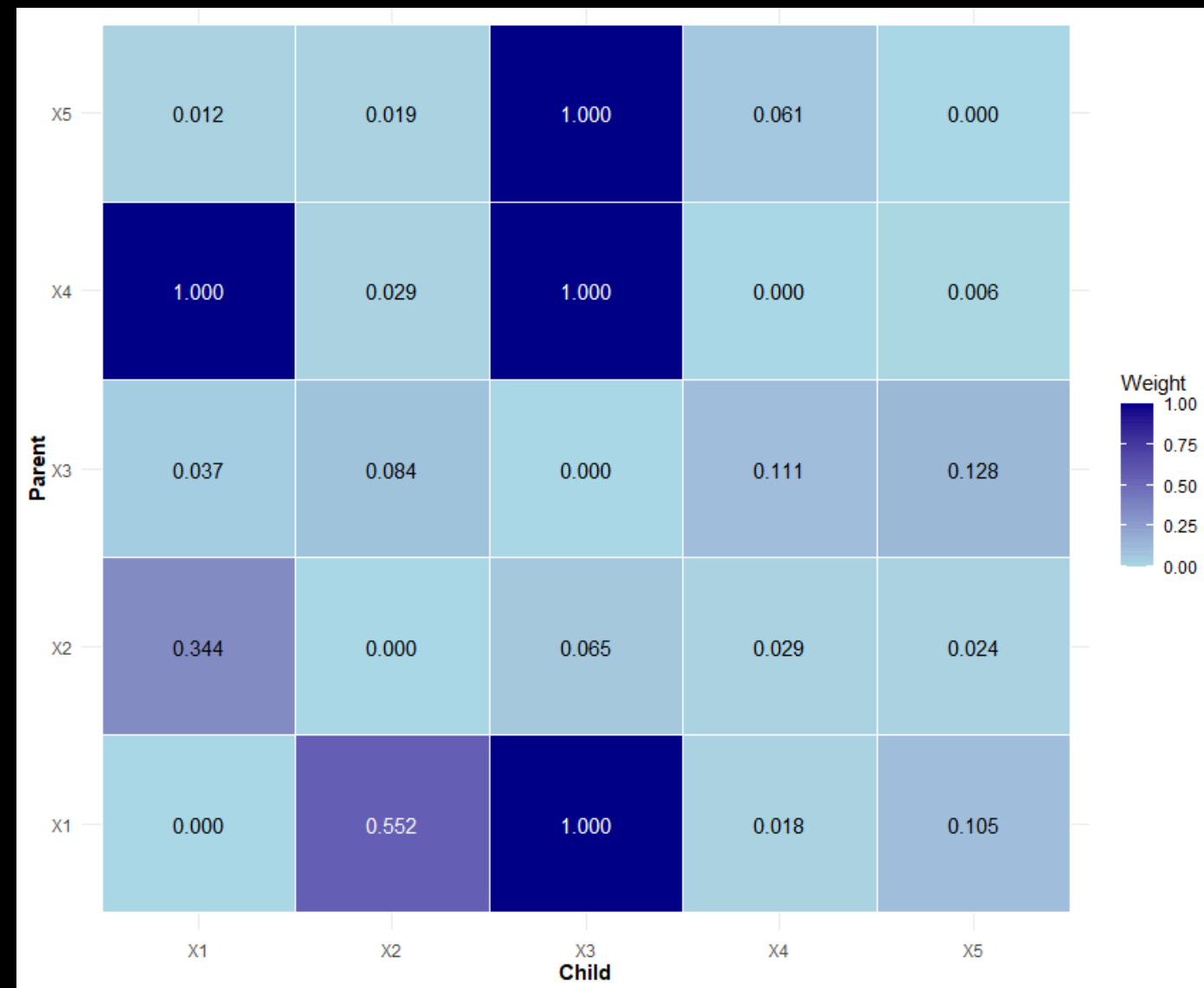
$$\begin{cases} \mu^* = \sigma^{2*} \cdot \left( \frac{\mu_i}{\sigma^{2(i)}} + \sum_{j:(X_i^t \in \pi_{(j)})} \beta_i^{(j)} \cdot \frac{x_j^{t+1} - \mu_{\{-i\}}^{(j)}}{\sigma^{2(j)}} \right) \\ \sigma^{2*} = \left( \frac{1}{\sigma^{2(i)}} + \sum_{j:(X_i^t \in \pi_{(j)})} \frac{(\beta_i^{(j)})^2}{\sigma^{2(j)}} \right)^{-1} \end{cases}$$

Sampling Missing Values iteratively from their FCD

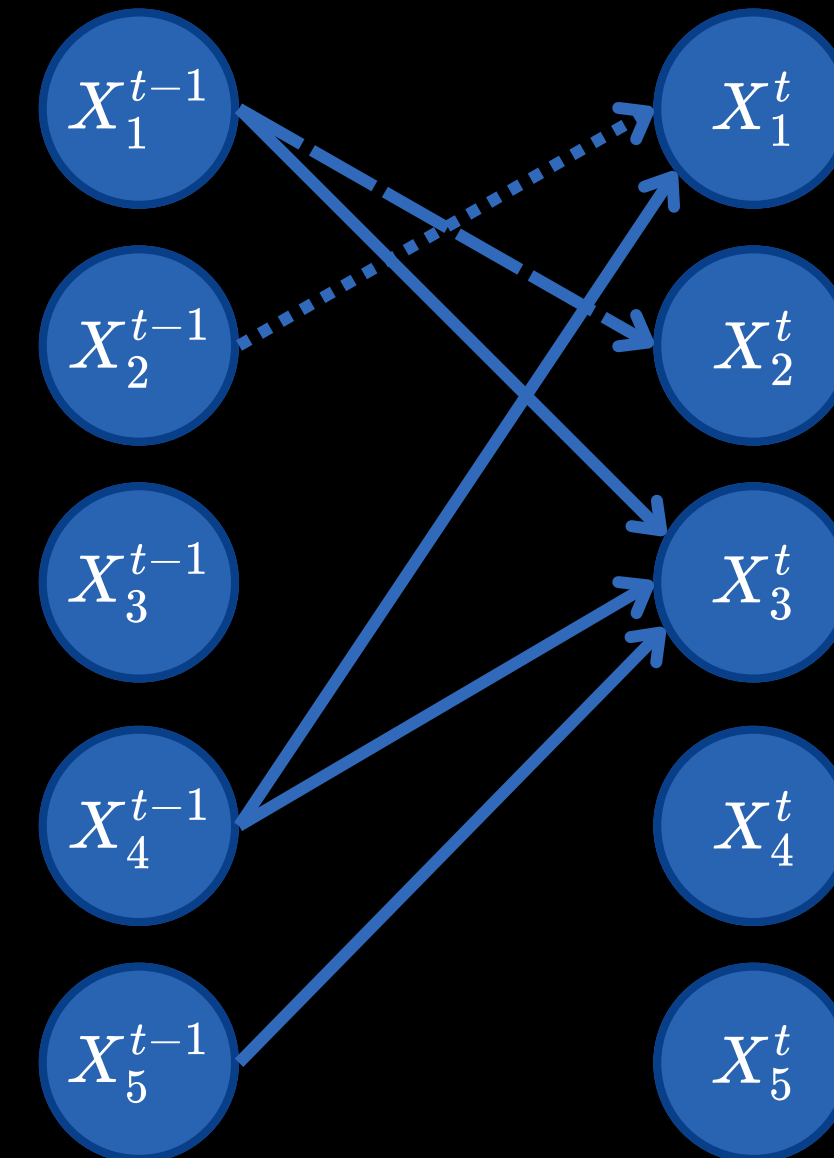
$$x_{i[MIS]} \sim \mathcal{N}(\mu^*, \sigma^{2*})$$

Conditional on  
the current  
structure and  
parameters

# Posterior Distributions



Edge Indicators Posteriors



DBN Structure

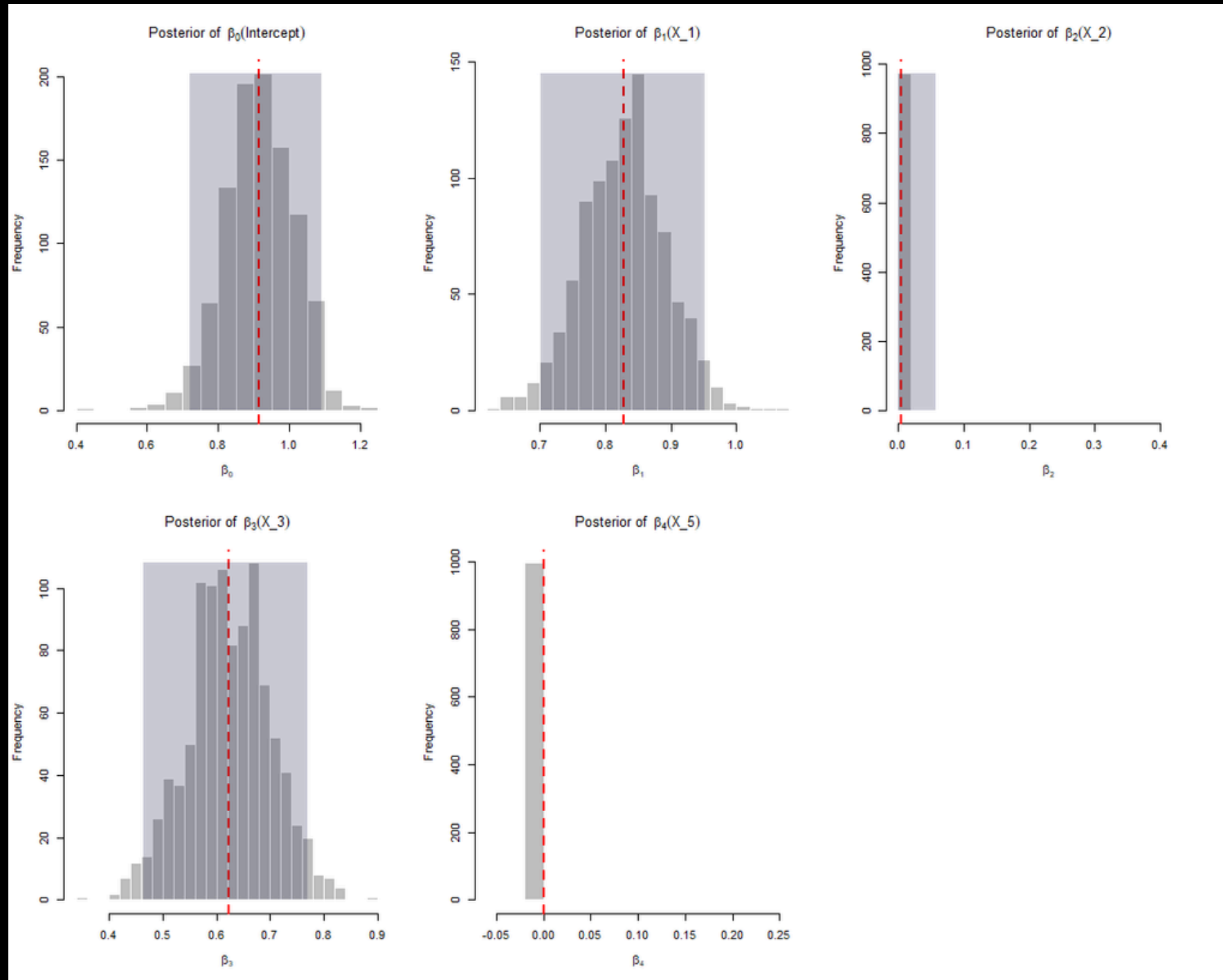
**FUN IN RESTRICTION** → KEEP ONLY THE LAST M SAMPLES (AFTER CONVERGENCE)

**THIN OUT STEP** → KEEP ONLY ONE SAMPLE EVERY  $\nu$  TO REDUCE AUTOCORRELATION

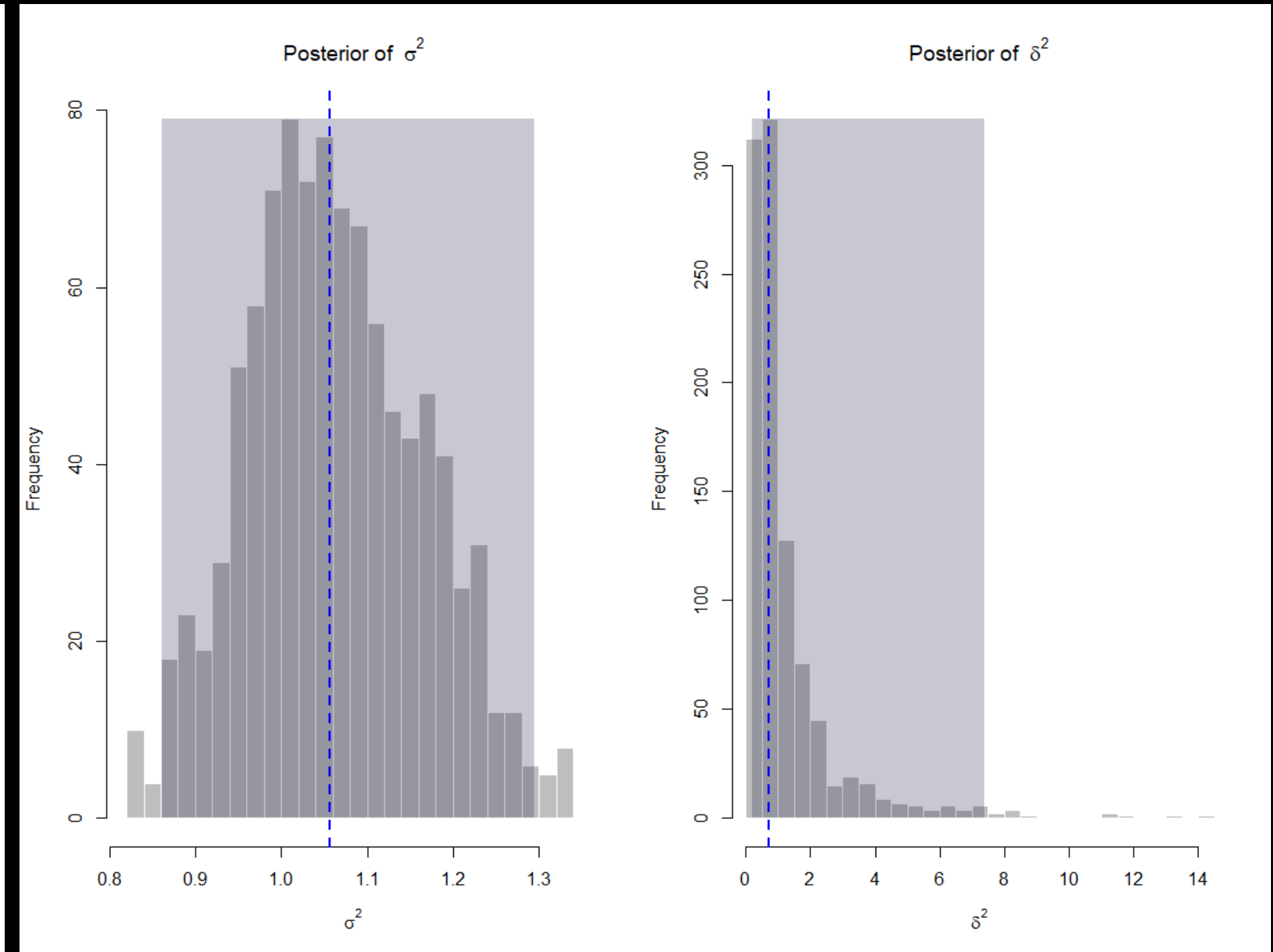


# Posterior Distributions

For each Bayesian Linear Regression:



Linear Coefficients Posteriors



Noise and Uncertainty Parameters Posteriors

# **Applications in Intensive Care**

# LUME-DBN Validation



**SIMULATION STUDIES**



**ICU CHALLENGE DATA**



**PREMATURITY CLINICAL DATA**

# LUME-DBN Validation



**SIMULATION STUDIES**



**ICU CHALLENGE DATA**



**PREMATURITY CLINICAL DATA**

+ DBN REFERENCE STRUCTURE AVAILABLE

+ DIFFERENT EXPERIMENTAL SCENARIOS

– DATA IS UNREALISTIC

# Simulated Experiments - Experimental Setting

To assess the validity of LUME-DBN both in terms of convergence and network reconstruction accuracy multiple incomplete datasets are generated from 10 distinct DBNs

## DBN GENERATION

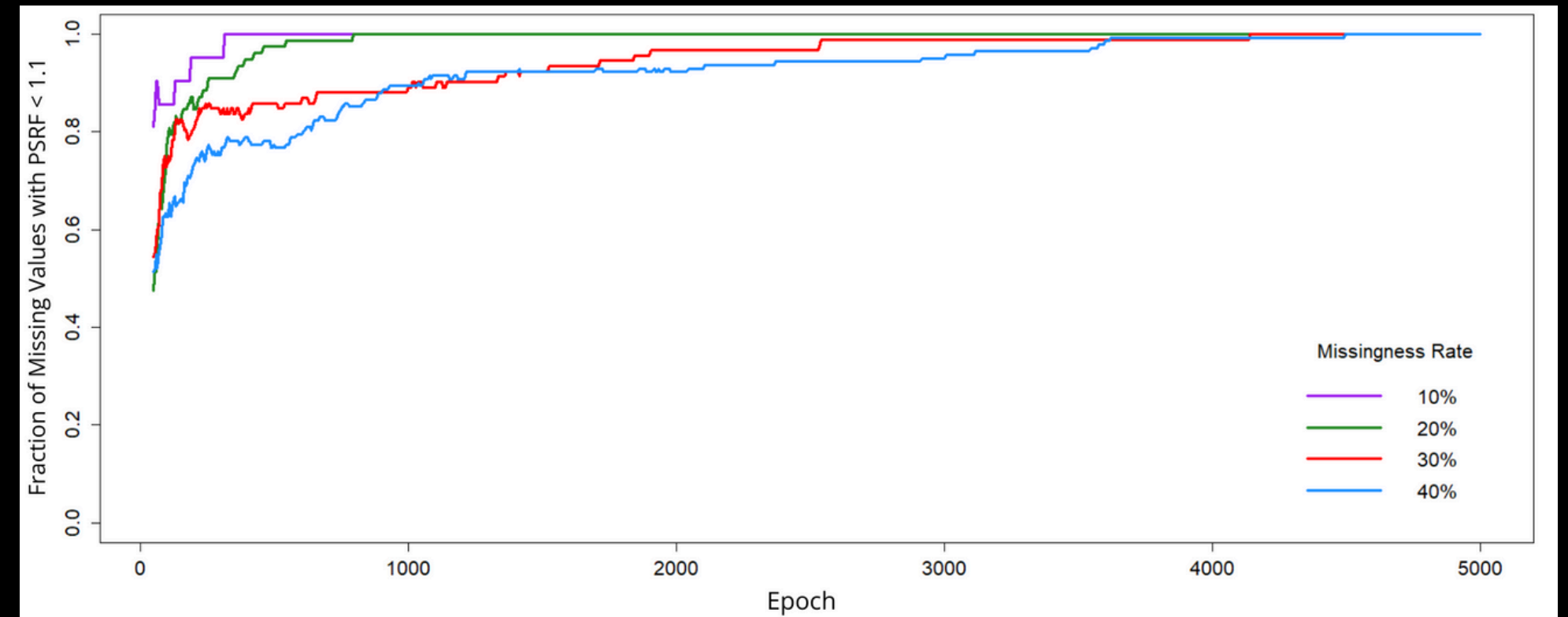
- **10 DBNs** with **10 nodes** and a maximum of 5 parents per node
- Random Topological Order to avoid
- Parameters:  $\beta \in U(0.2, 0.5) - \sigma^2 = 1$

## DATA GENERATION

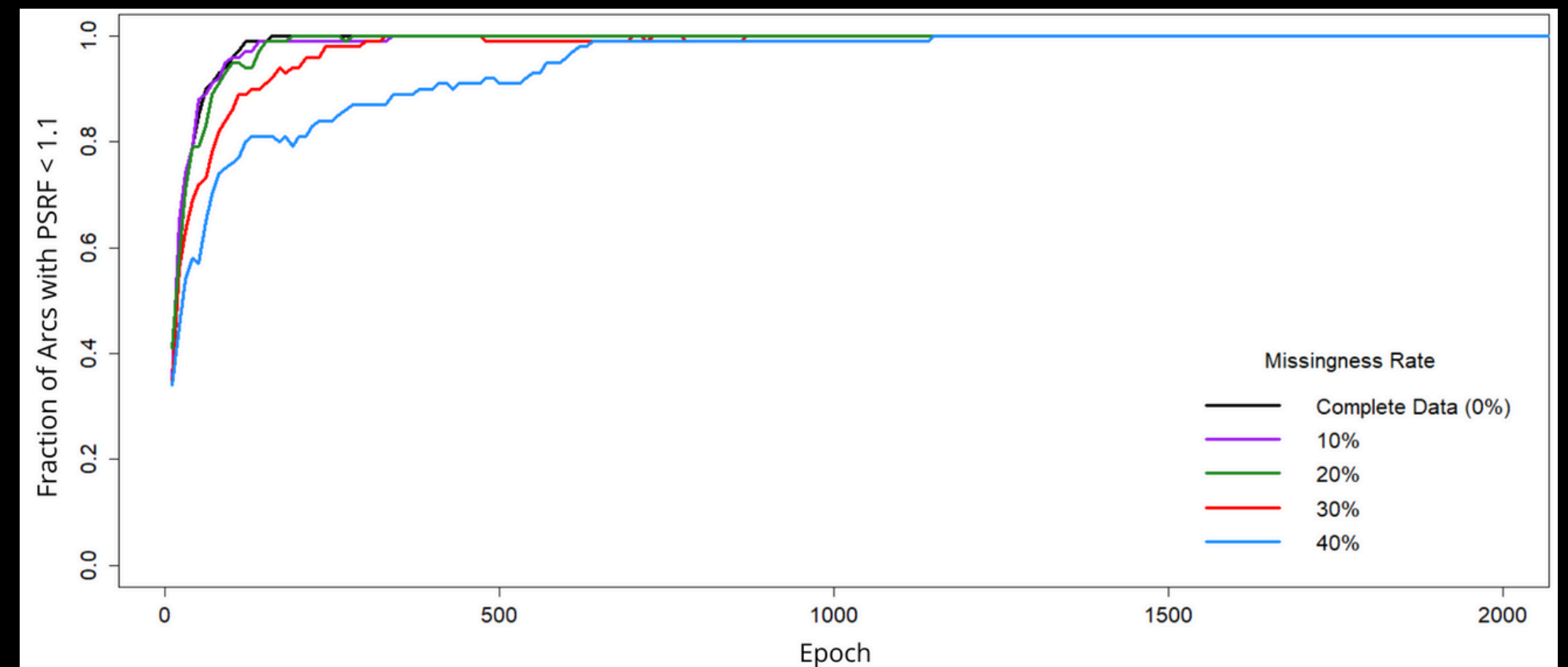
- For each DBN a set of random time series is generated with 3 sample sizes:  $T = \{50, 100, 200\}$
- For each complete Dataset 4 incomplete dataset are generated at 4 sample sizes:  $\{0.1, 0.2, 0.3, 0.4\}$

# Simulation Results - Convergence Diagnostics

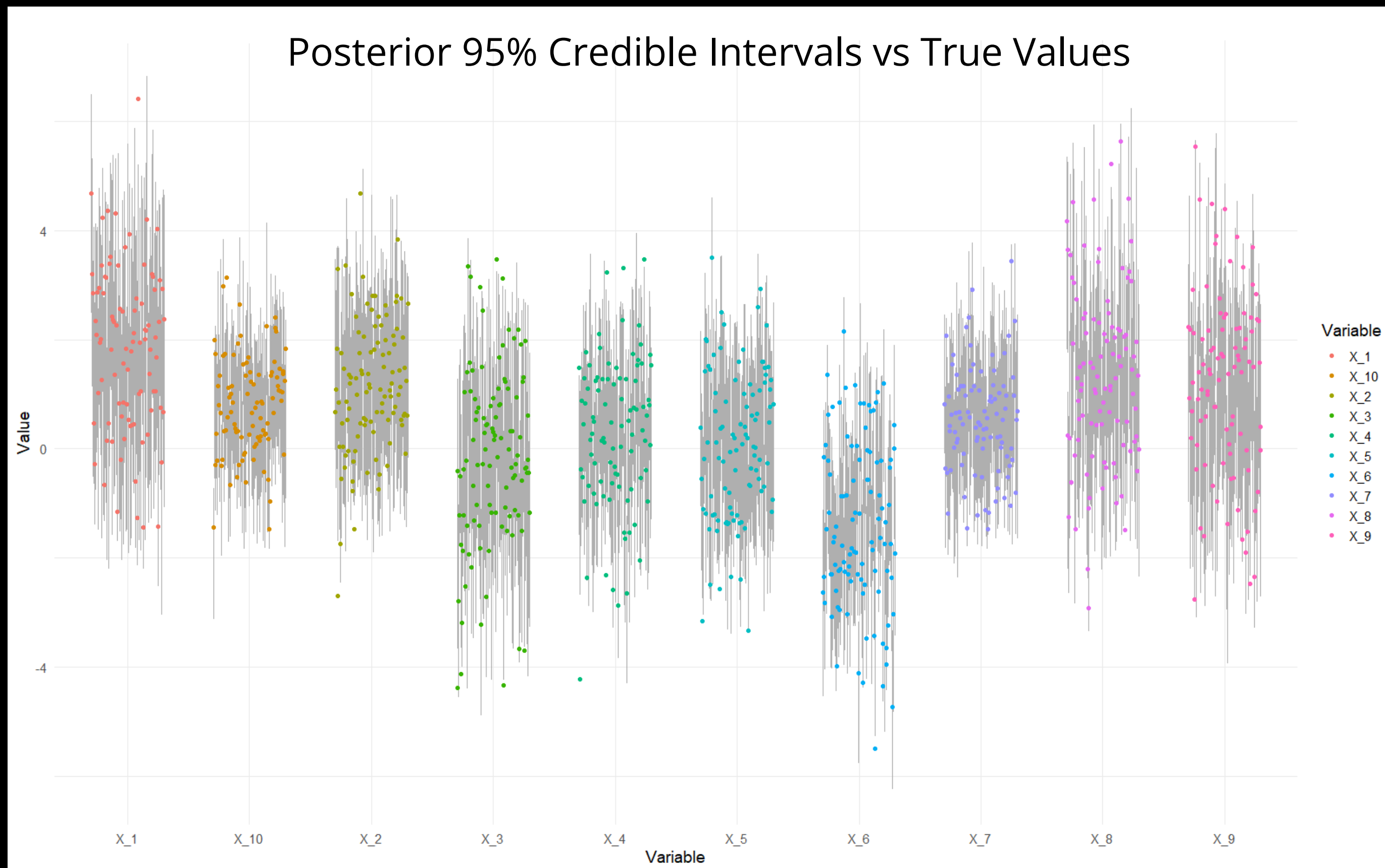
The convergence of the **DBN structure** and the **missing values** is evaluated in **terms of potential scale reduction factors** along parallel simulations



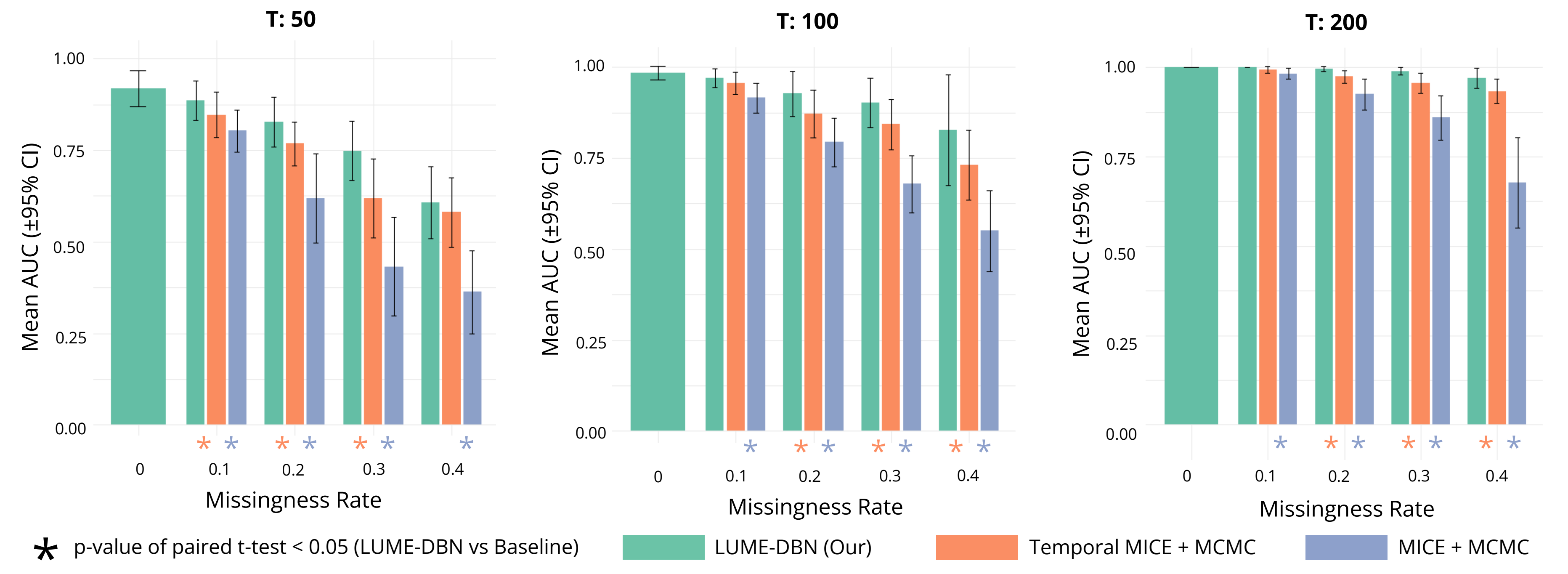
**Convergence** is reached when the **proportion of posterior samples** with **PSRF < 1.1** consistently **reaches 1**



# Simulation Results - 95% Credible Intervals for Missing Values



# Simulation Results - Network Reconstruction Accuracy





# LUME-DBN Validation



SIMULATION STUDIES



ICU CHALLENGE DATA



PREMATURITY CLINICAL DATA

- + REAL-WORLD RETROSPECTIVE DATA
- + DATA FROM MULTIPLE FACILITIES
- UNKNOWN DATA COLLECTION PROCEDURE
- NO REFERENCE STRUCTURE

# A case study in Critical Care - The Physionet 2012 Dataset

## PHYSIONET DATABASE

- Records from 20k patients admitted to the ICU
- Data acquired in the first 48 hours of ICU stay

## SAMPLE SELECTION

- Including severe patients only (SOFA score  $> 12$ )
- Stratification based on ICU types



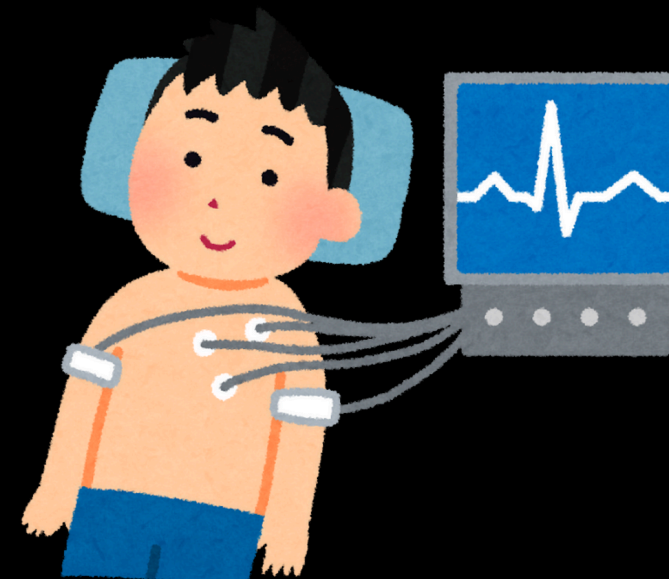
**MEDICAL ICU (MICU)**

34 patients



**SURGICAL ICU (SICU)**

104 patients



**CORONARY CARE (CCU)**

114 patients



**CARDIAC SURGERY (CSRU)**

62 patients

# A case study in Critical Care - Different Standardization Techniques

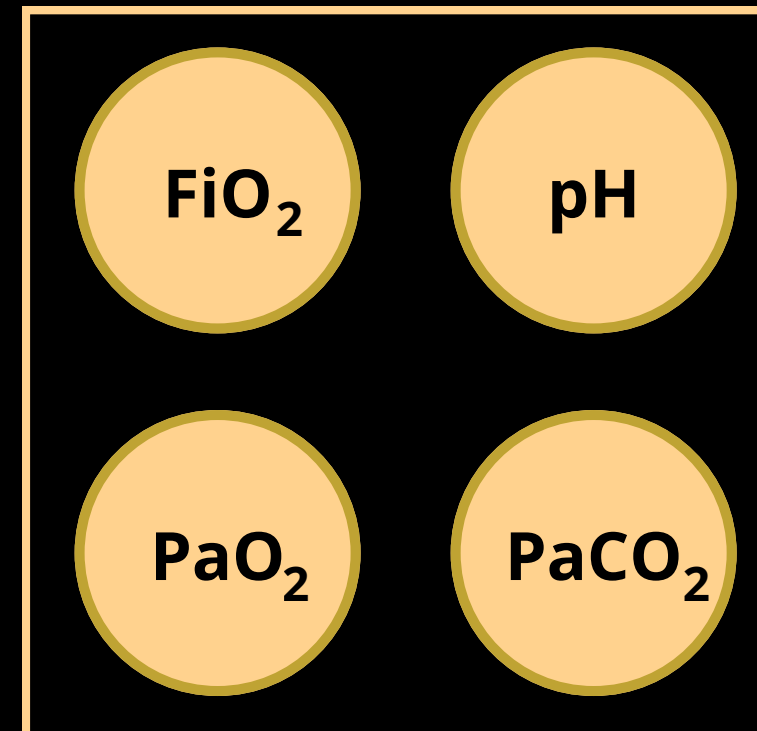
## TEMPORAL DISCRETIZATION

- Discretization into 6-hour intervals ( $T = 9$ )
- Keeping the variables with missingness rates  $< 40\%$  compatible with the experimental results

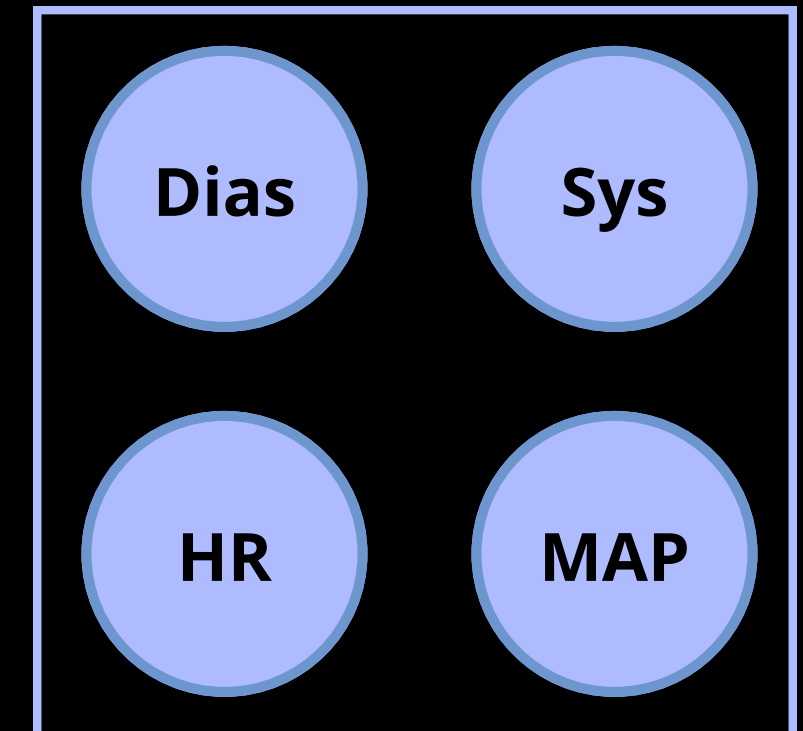
## STANDARDIZATION

- Local Standardization: applied for each ICU group
- Global Standardization: on the whole dataset

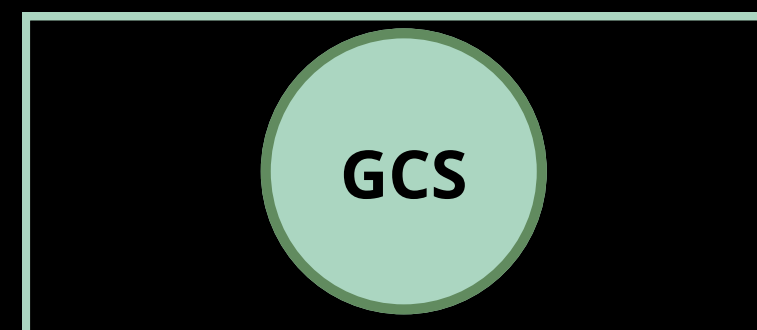
### RESPIRATORY



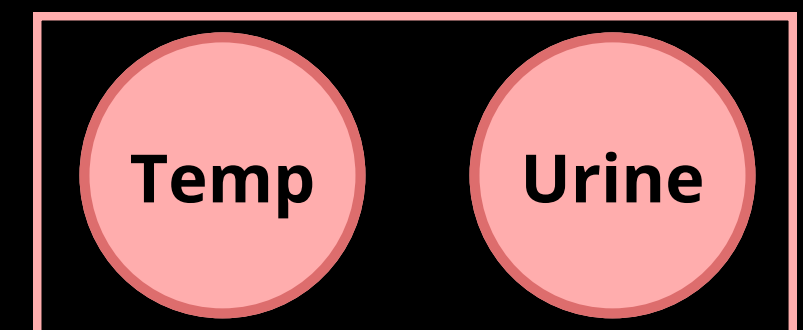
### VITAL PARAMETERS



### NEUROLOGICAL

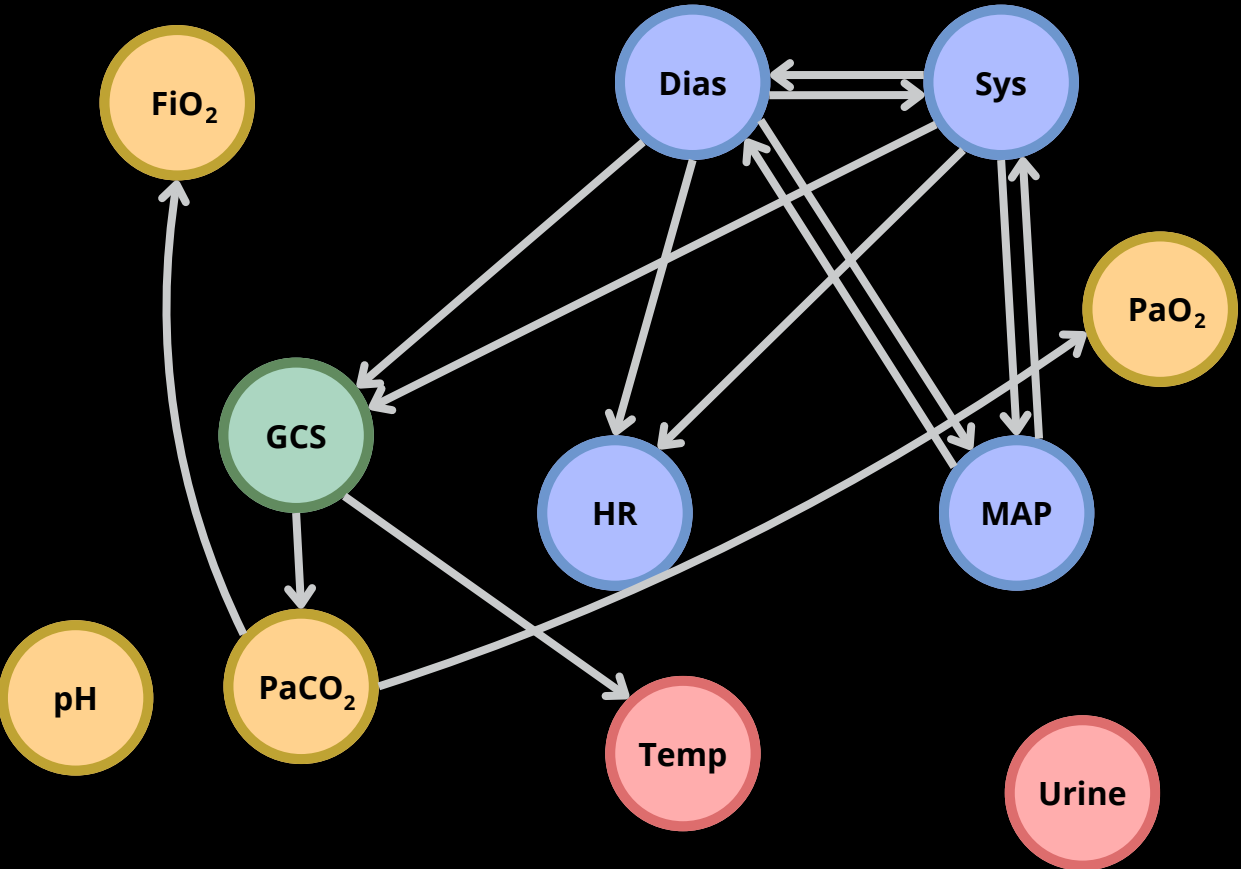


### PHYSIOLOGICAL

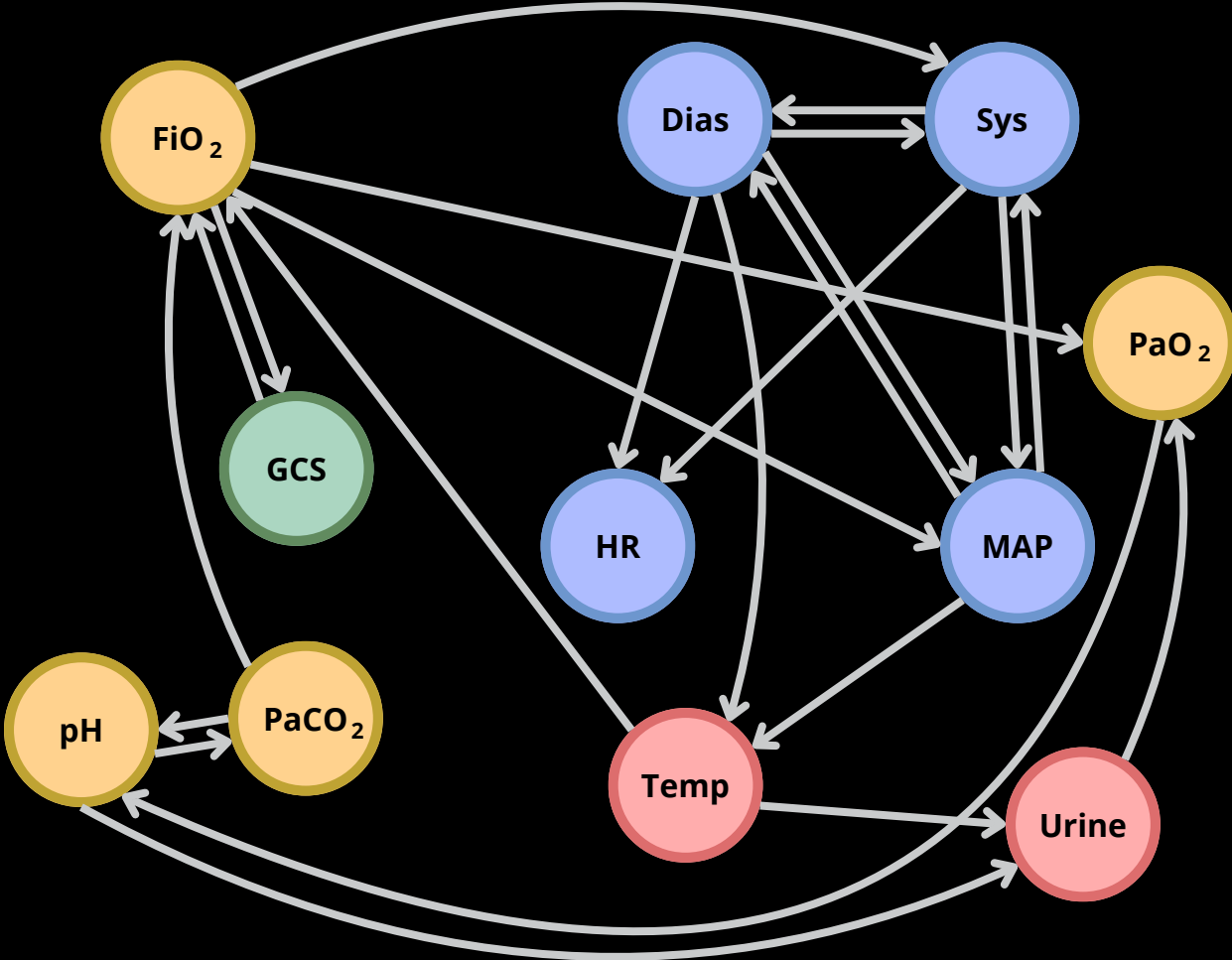


# Commonalities and Differences between group-specific DBNs

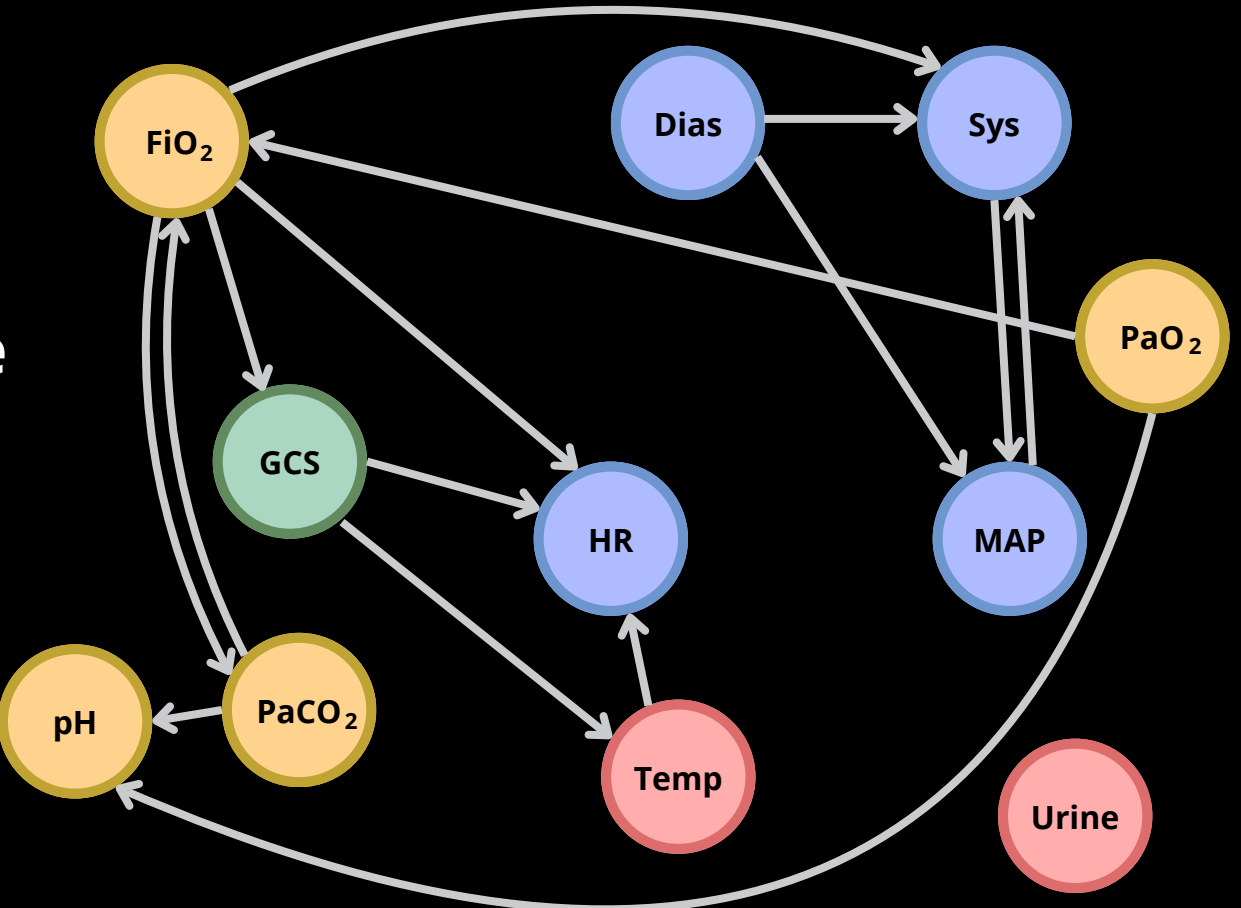
Medical ICU (MICU)



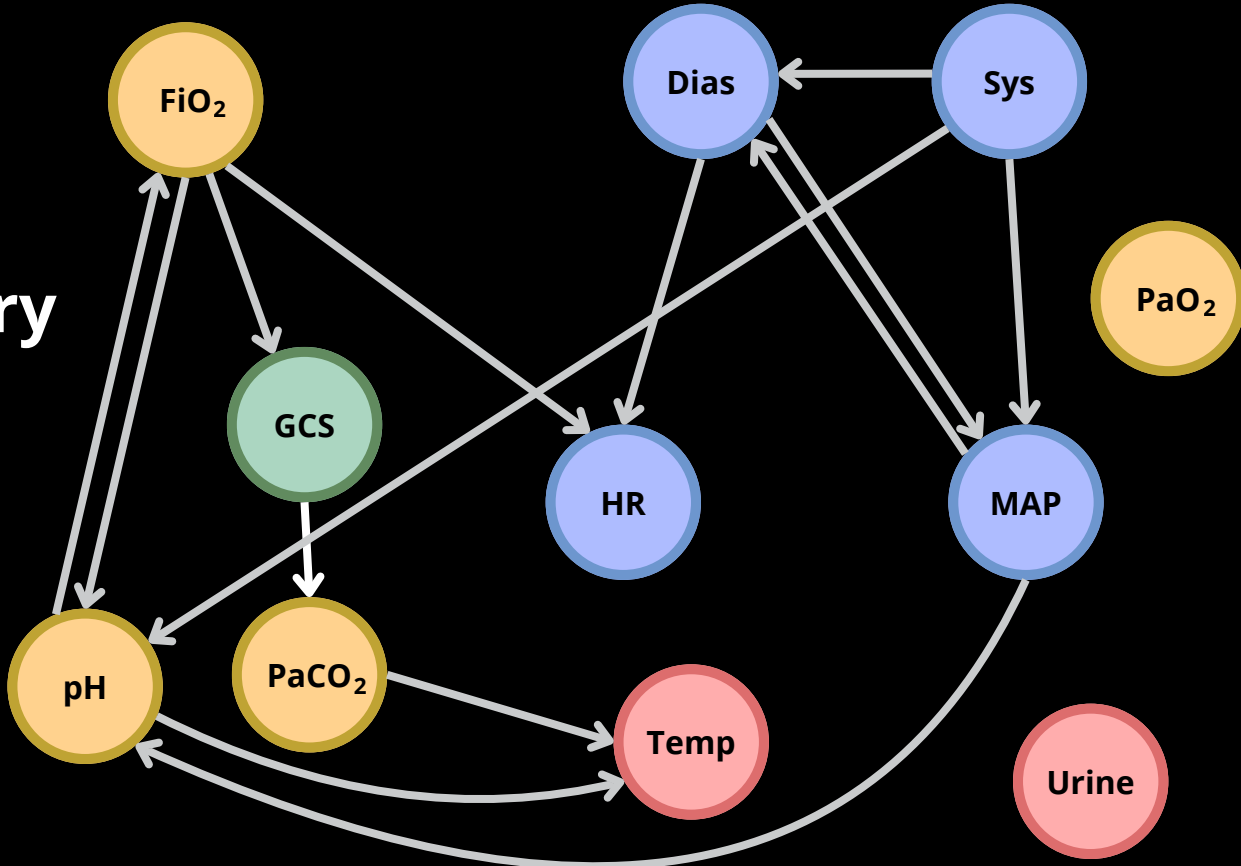
Surgical ICU (SICU)



Coronary Care (CCU)

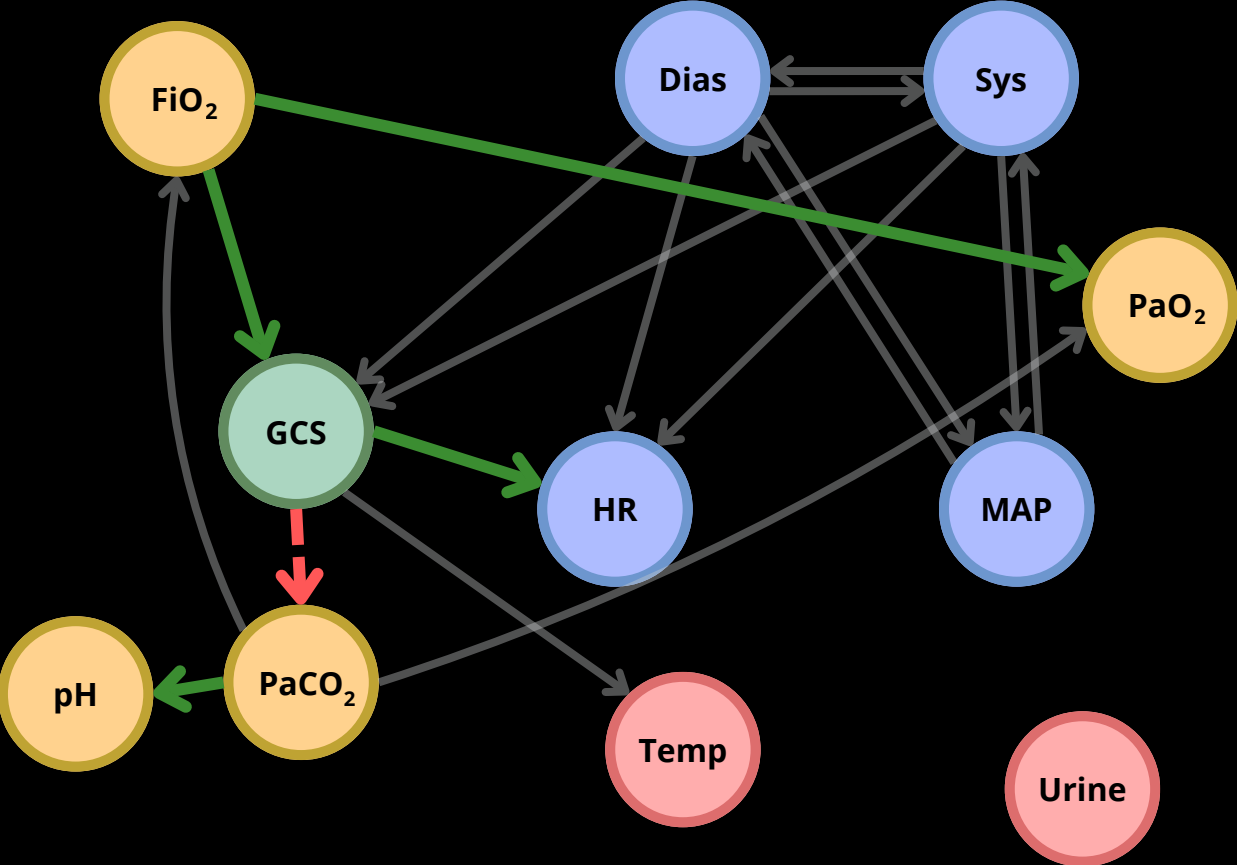


Cardiac Surgery (CSRU)

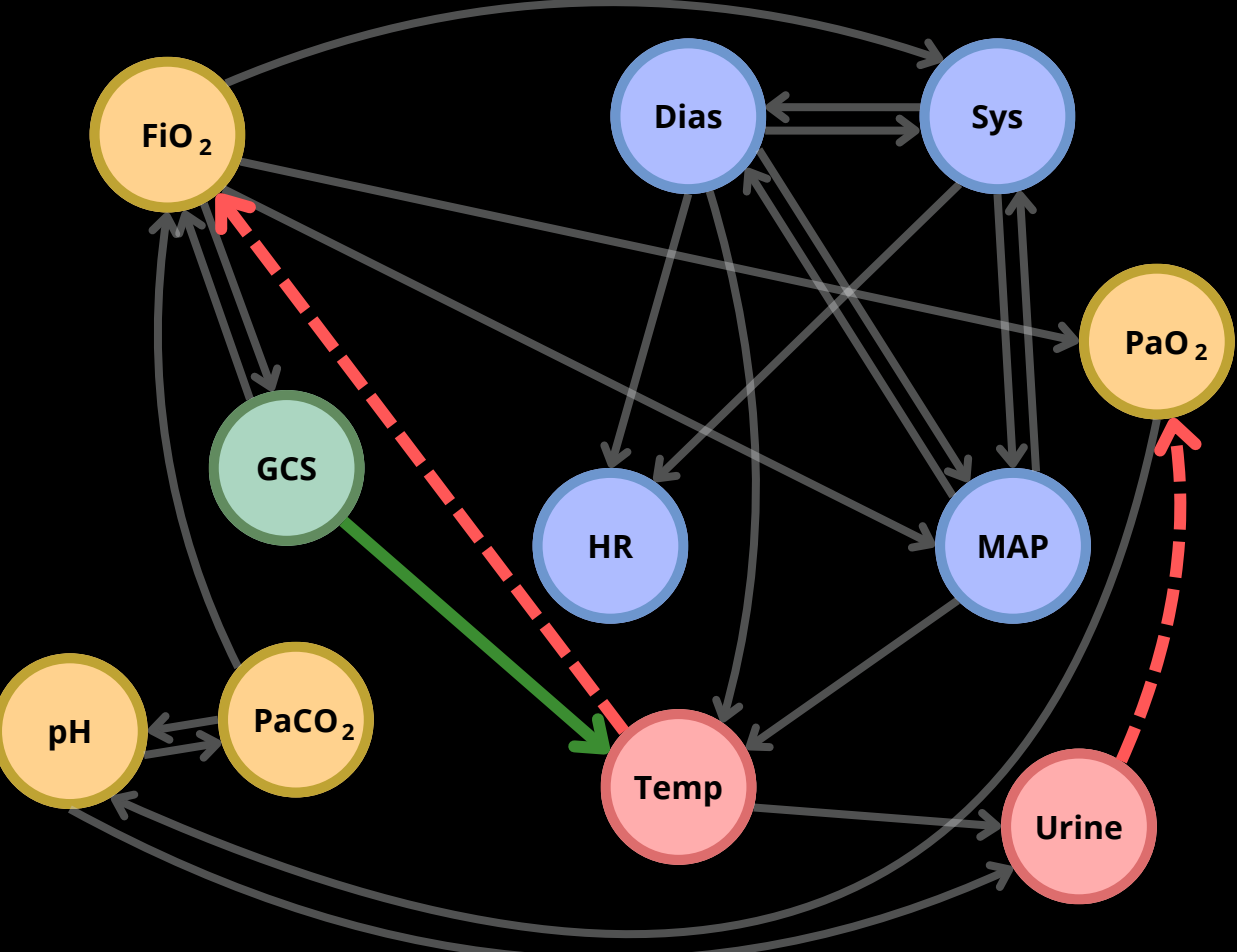


# Results with different Standardization Techniques

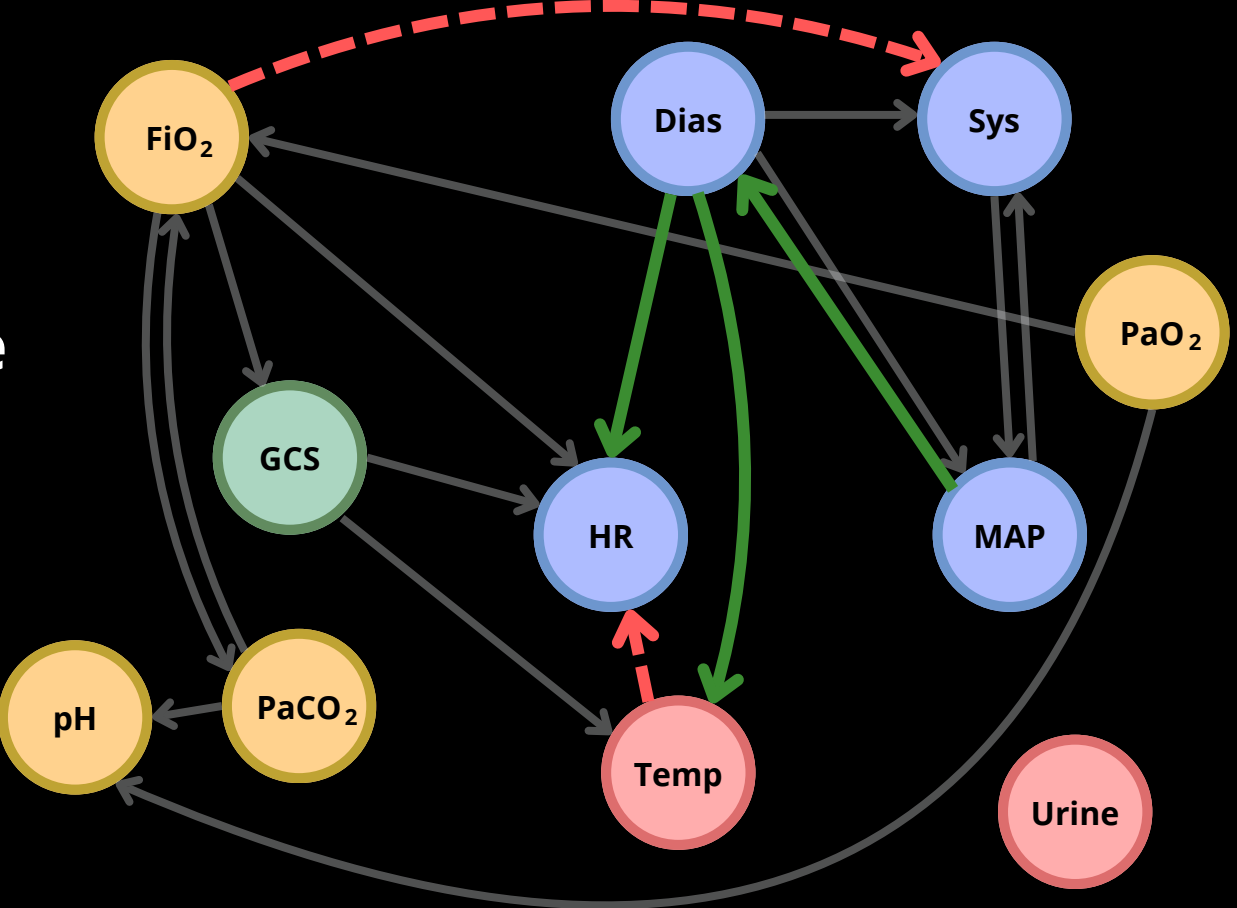
Medical ICU (MICU)



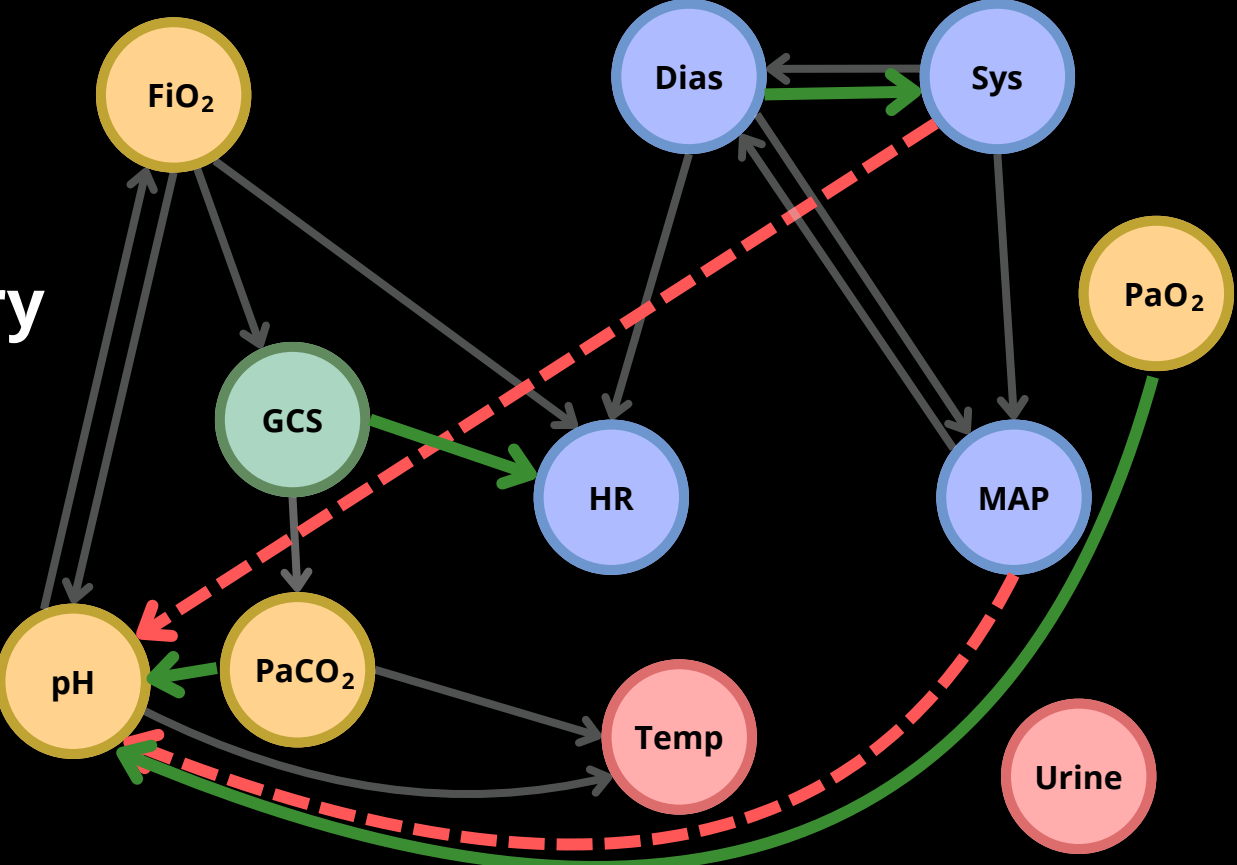
Surgical ICU (SICU)



Coronary Care (CCU)



Cardiac Surgery (CSRU)



Global Standardization Only  
Local Standardization Only



# LUME-DBN Validation



SIMULATION STUDIES



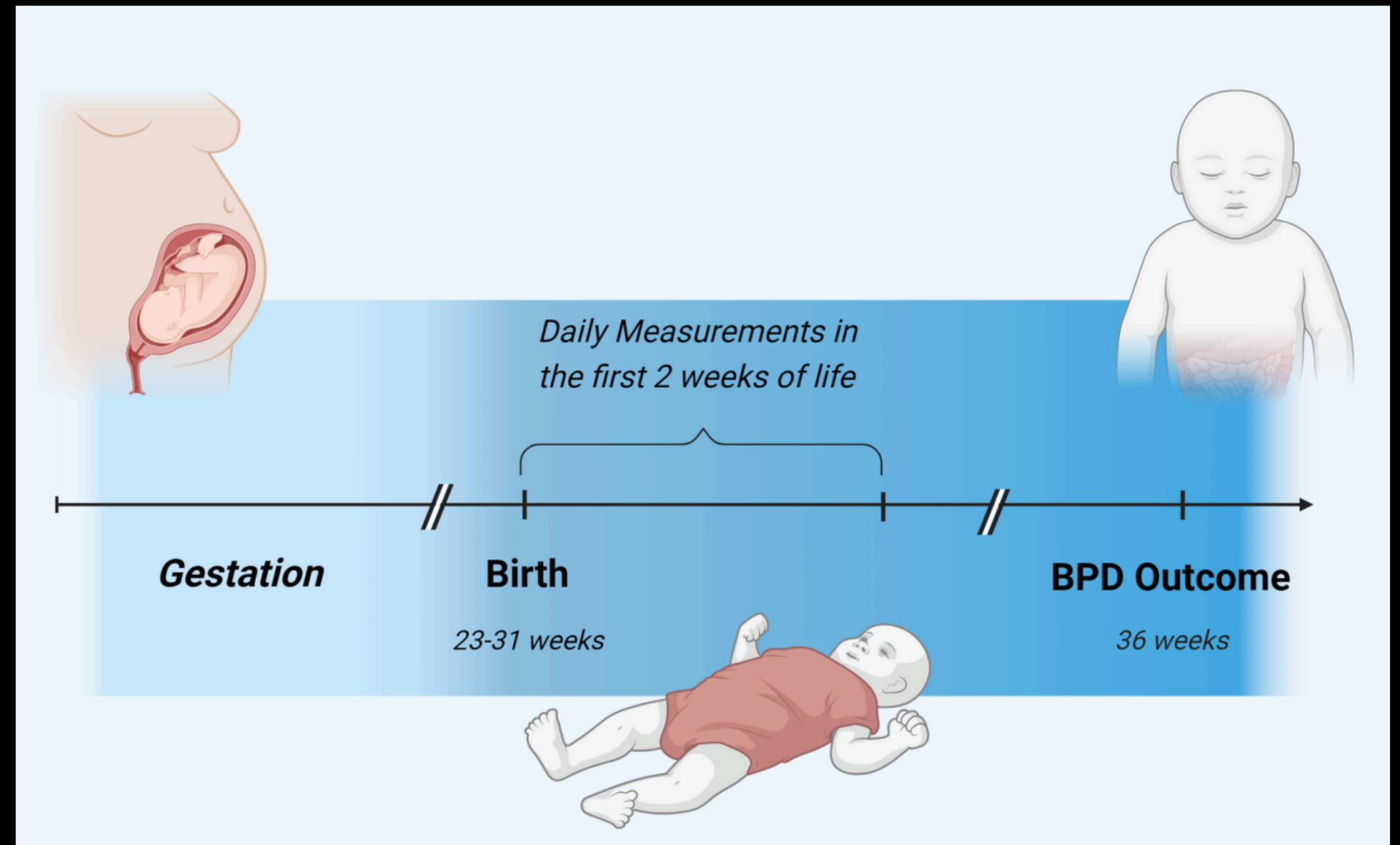
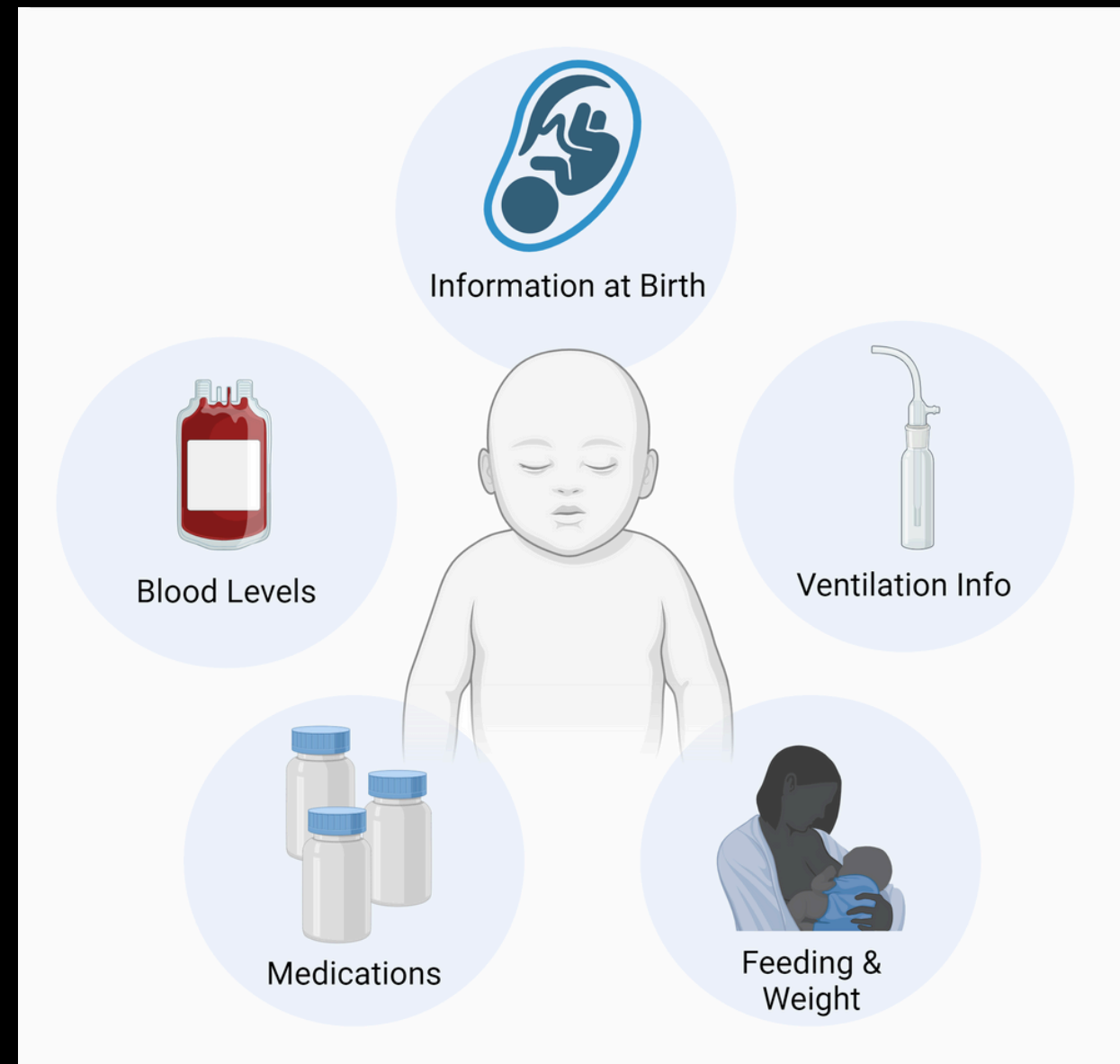
ICU CHALLENGE DATA



PREMATURITY CLINICAL DATA

- + REAL-WORLD RETROSPECTIVE DATA
- + KNOWN DATA COLLECTION PROCEDURE
- + CLINICAL DOMAIN KNOWLEDGE
- NO REFERENCE STRUCTURE

# A case study on Bronchopulmonary Dysplasia



A multidisciplinary project in collaboration with the neonatologist of the TIN Mangiagalli with the aim of early detecting BPD and understanding respiratory dynamics in extremely and very preterm newborns

# Data Preprocessing

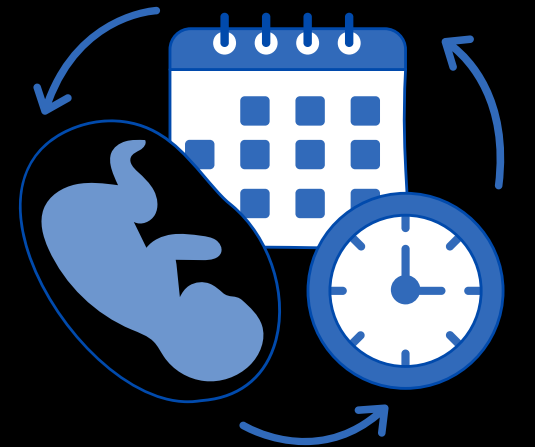
## DATA COLLECTION

- Patients born from 2017 to 2022 with gestational age (GA) < 32 weeks and birth weight <1500 g
- Data extraction from the Electronic Medical Records (EMR)



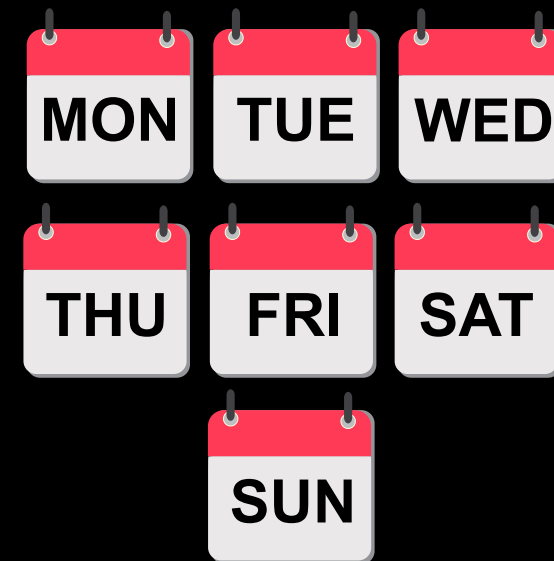
## SAMPLE SELECTION

- Excluding patients with congenital malformations and outborns
- Ruling out patients not disposing of BPD outcomes at 36 weeks



## DISCRETIZATION

- Time discretization aggregating dynamic data on a daily basis (cumulative dosages, median ventilation and blood parameters)



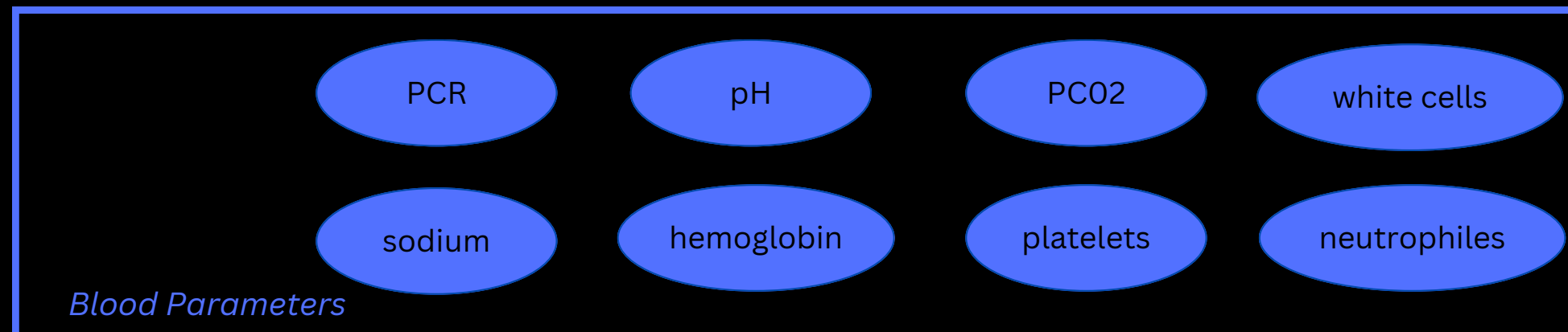
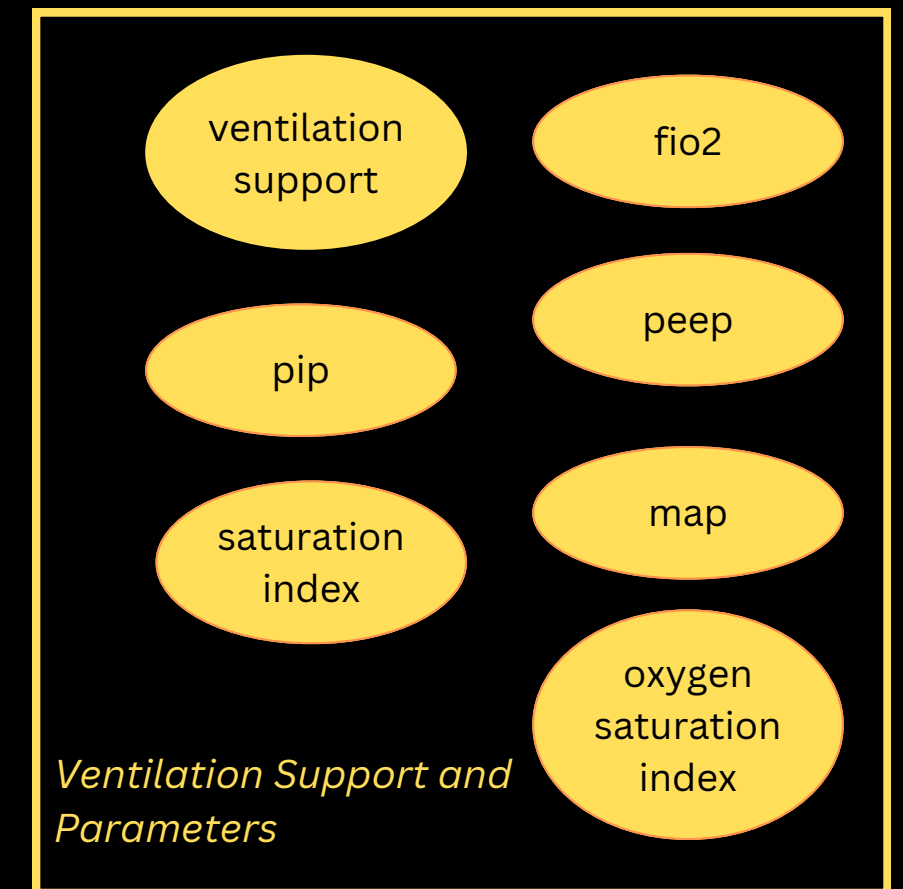
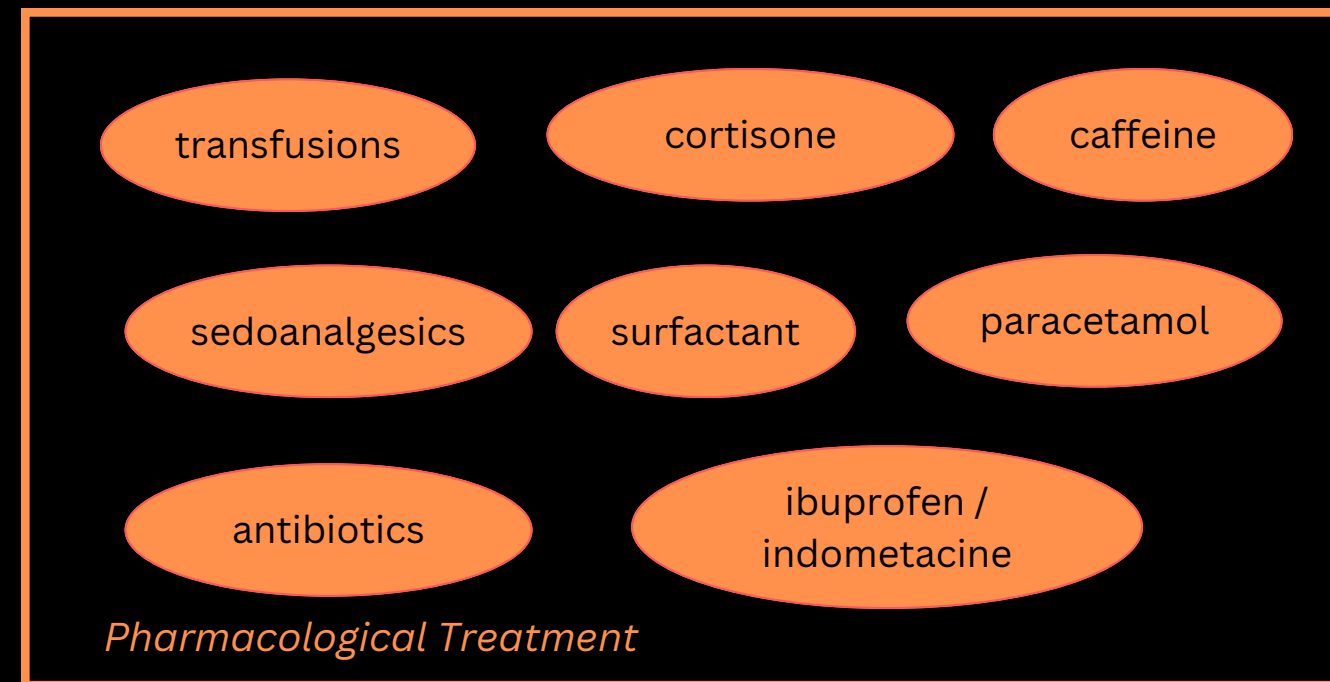
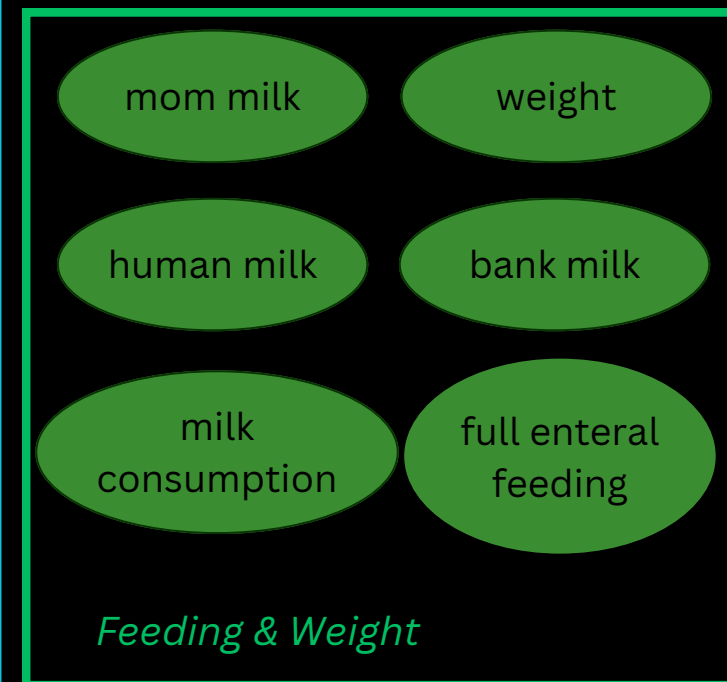
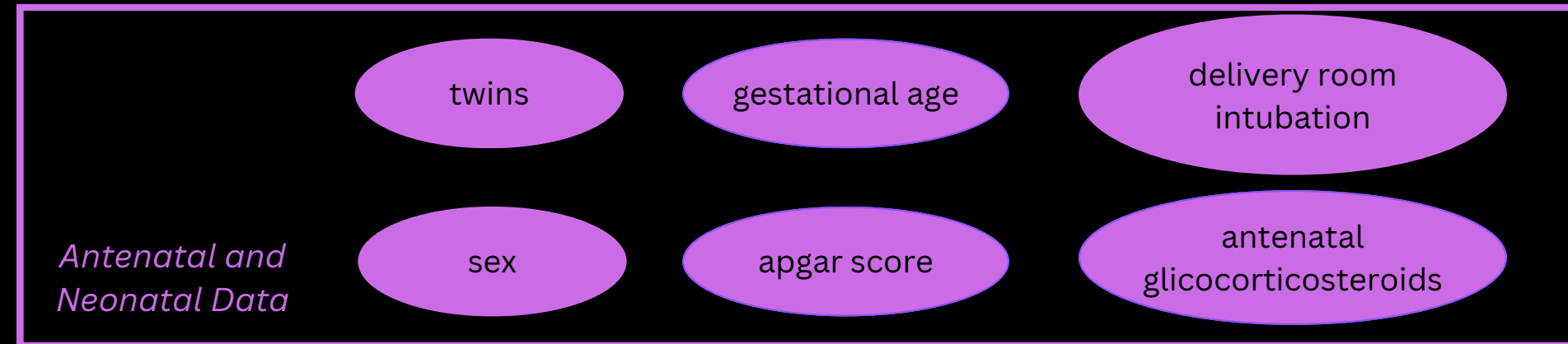
## DATA CLEANING

- Validation of the features ranges based on laboratory thresholds
- The resulting dataset is comprised of mixed static and temporal data from 461 babies (287 healthy and 174 BPD)





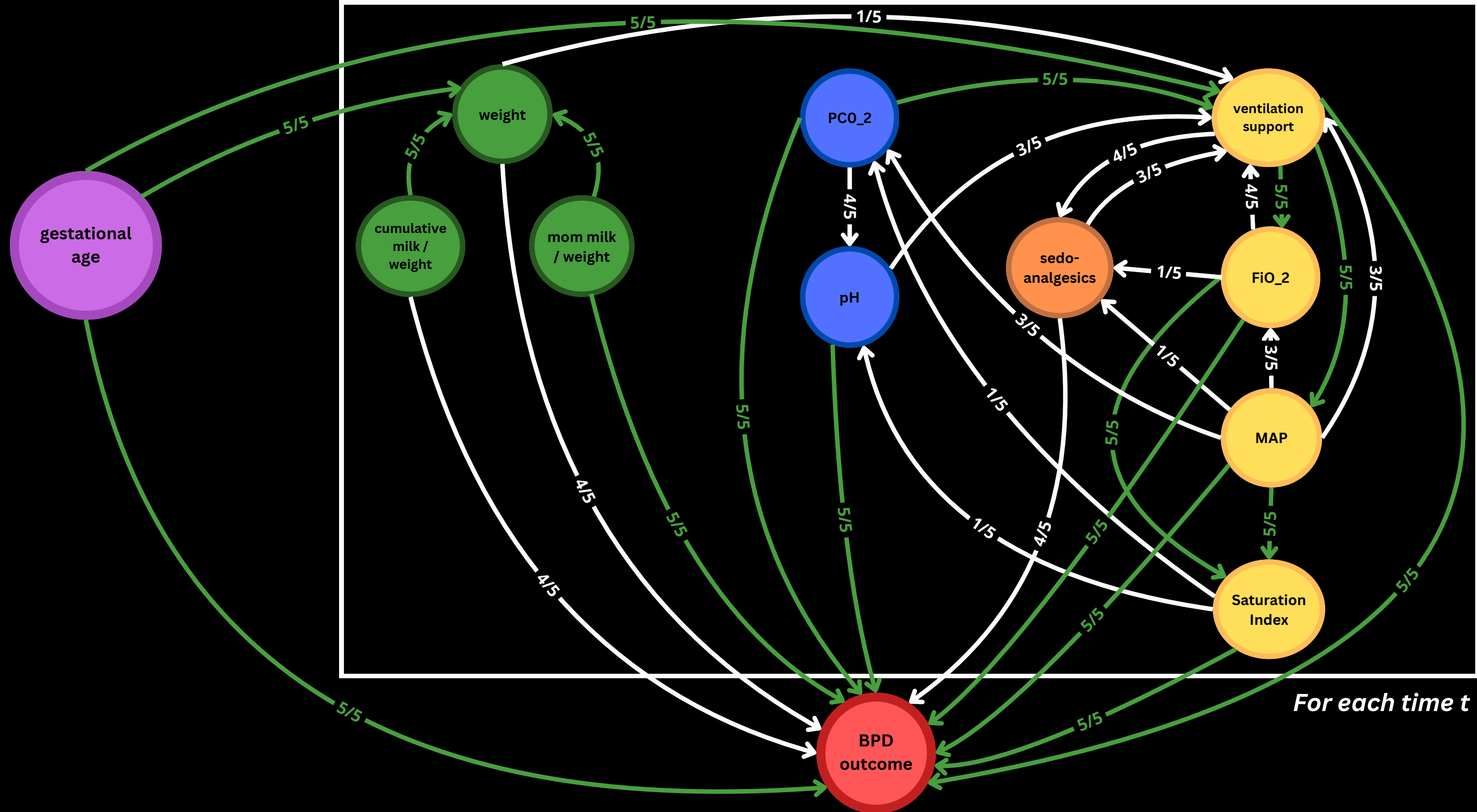
# Incorporating prior structural knowledge



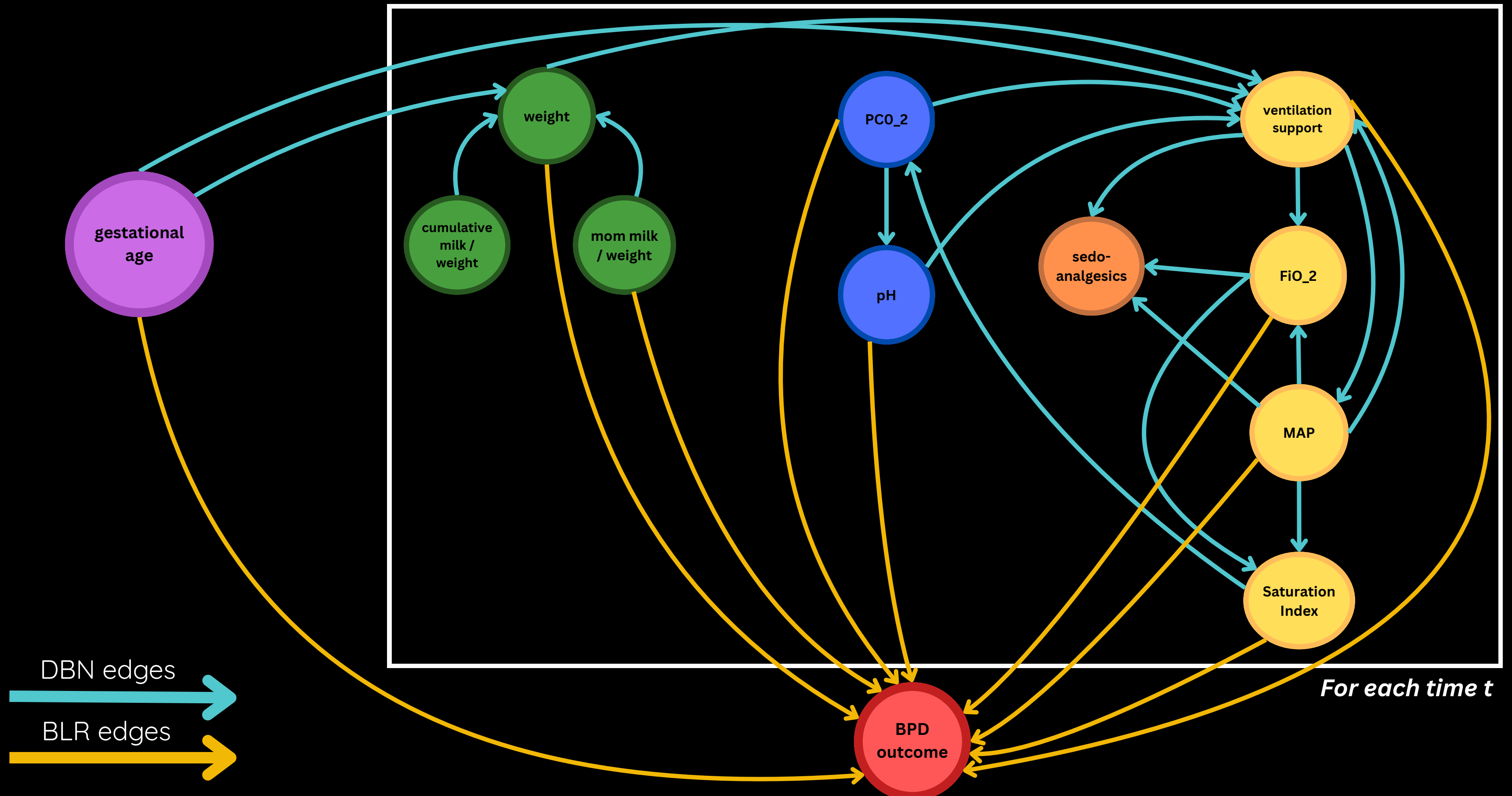
*For each time  $t$*



# Prior informed DBN + Bayesian Logistic Regression (BLR) learning

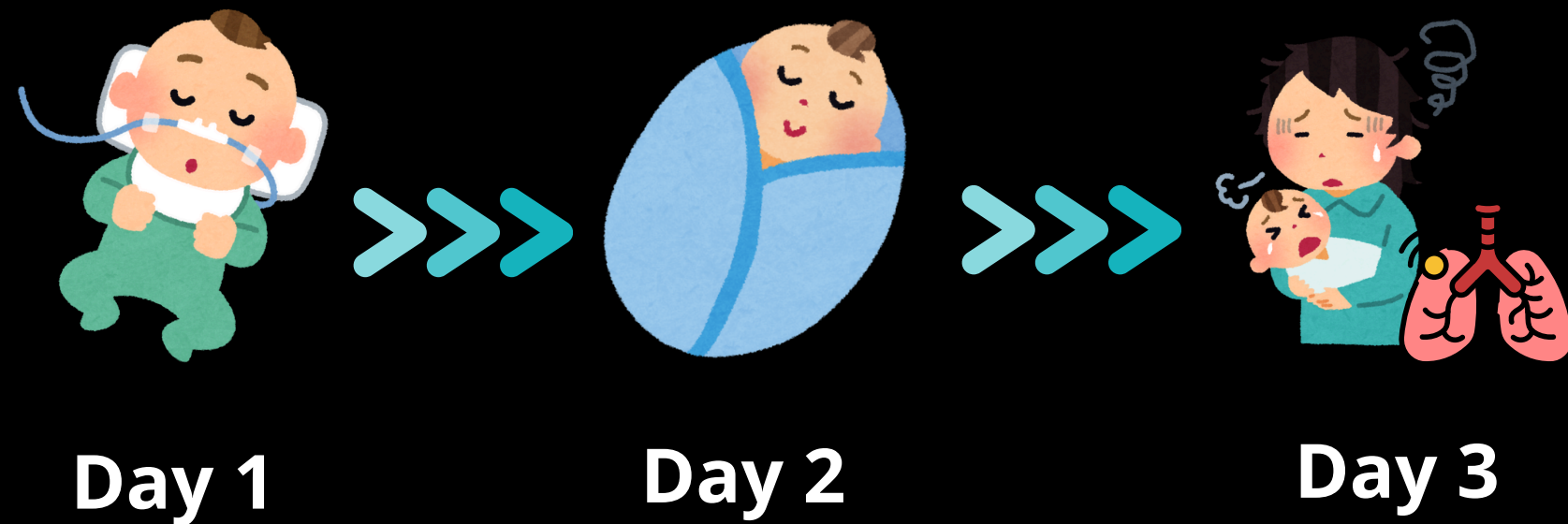


# Expert-informed Learning of DBN + BLR

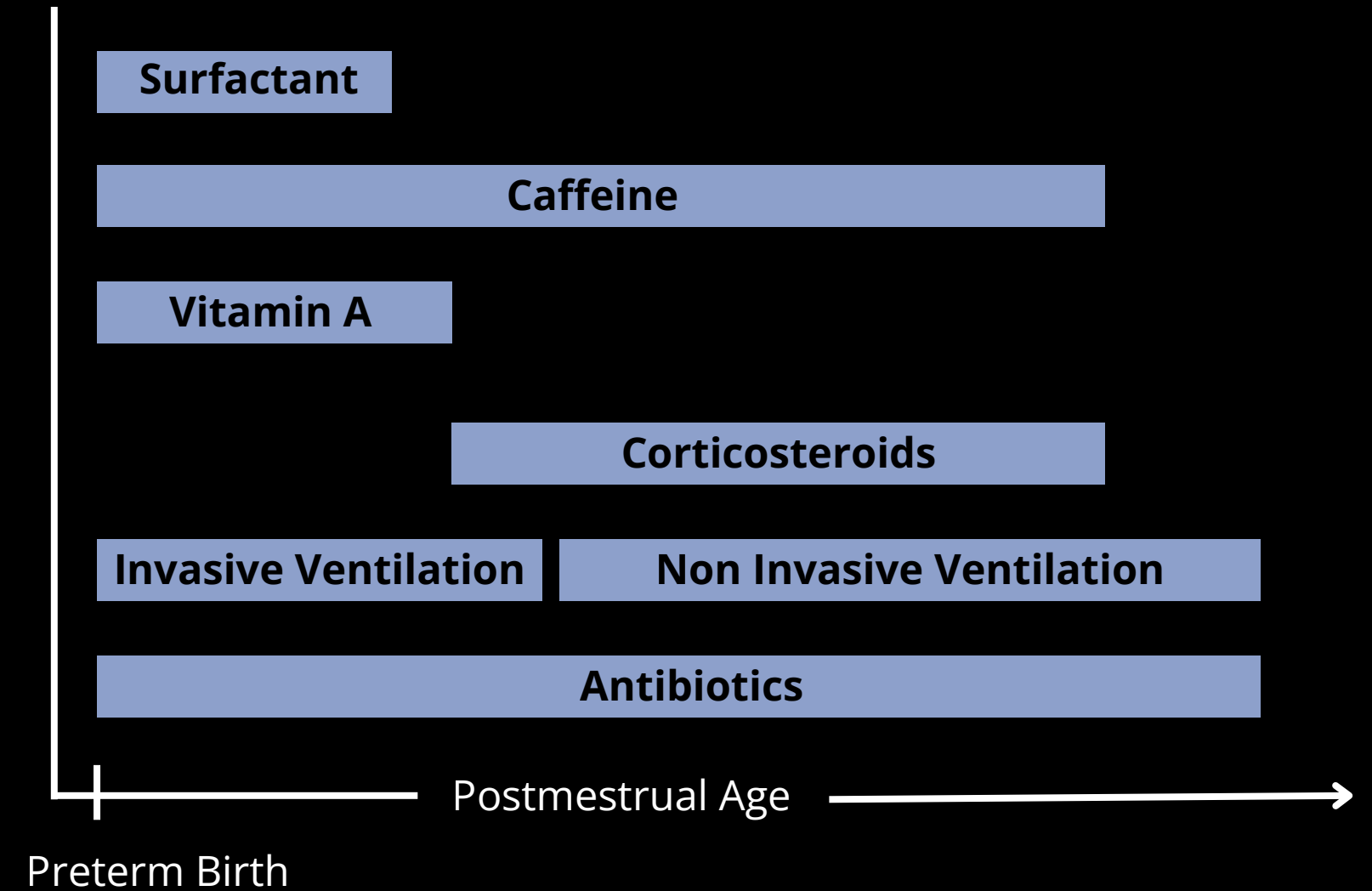


**Why Standard (Homogeneous) DBNs  
could be suboptimal?**

# Temporal Shifts in System Dynamics



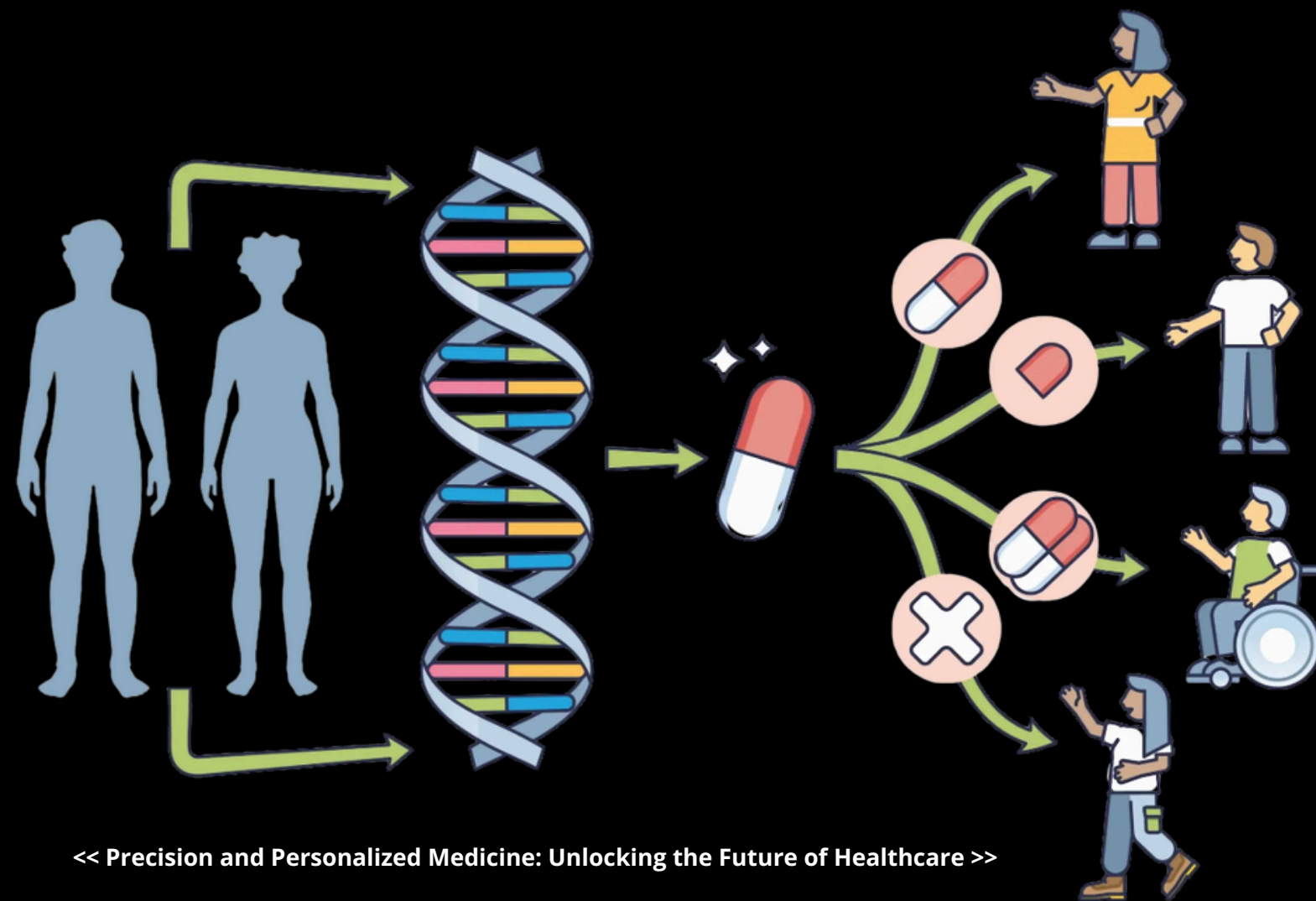
*Unstable patients condition in the first few weeks of life*



*European standards for treatment adoption in premature newborns*

**Evolving temporal mechanism identification towards a better patient care over time**

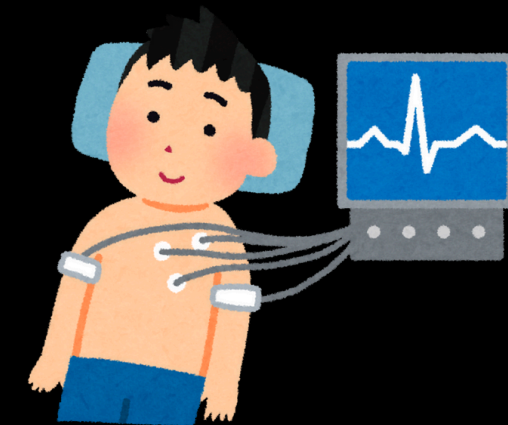
# Deviation in treatment effects across patients groups



MEDICAL ICU (MICU)



SURGICAL ICU (SICU)



CORONARY CARE (CCU)



CARDIAC SURGERY (CSRU)

*Treatment Effects changing from patient to patient*

*Distinct Groups of Patients with diverse conditions*

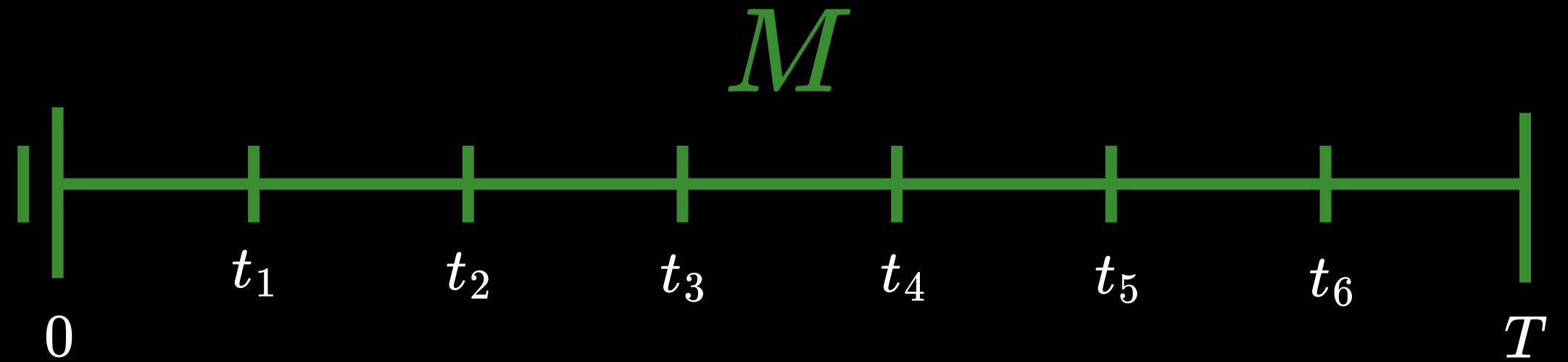
**Varying dynamics identification across different groups towards personalize patient care**

# Non-stationary Temporal Models



# Non-stationary Temporal Models

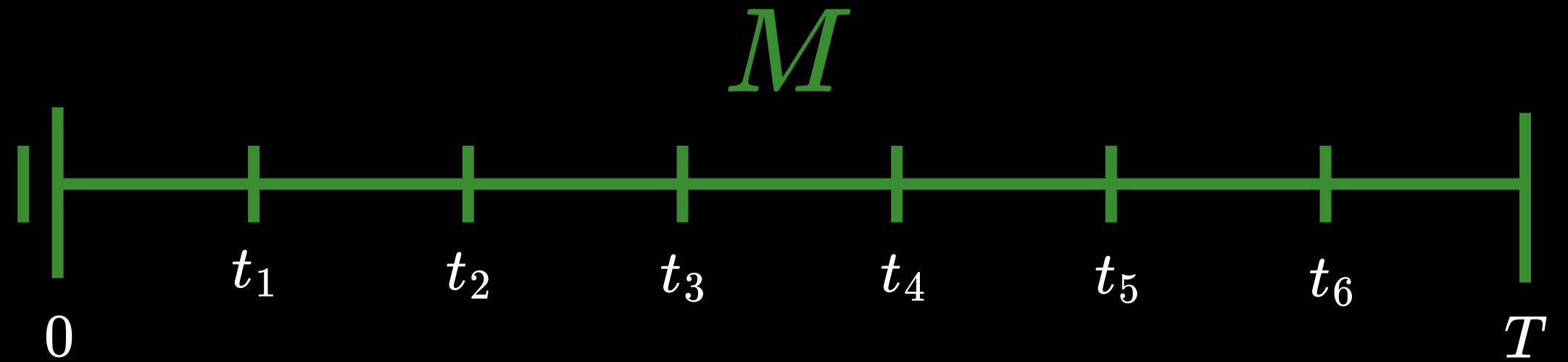
STATIONARY MODEL ACROSS  
THE WHOLE PERIOD



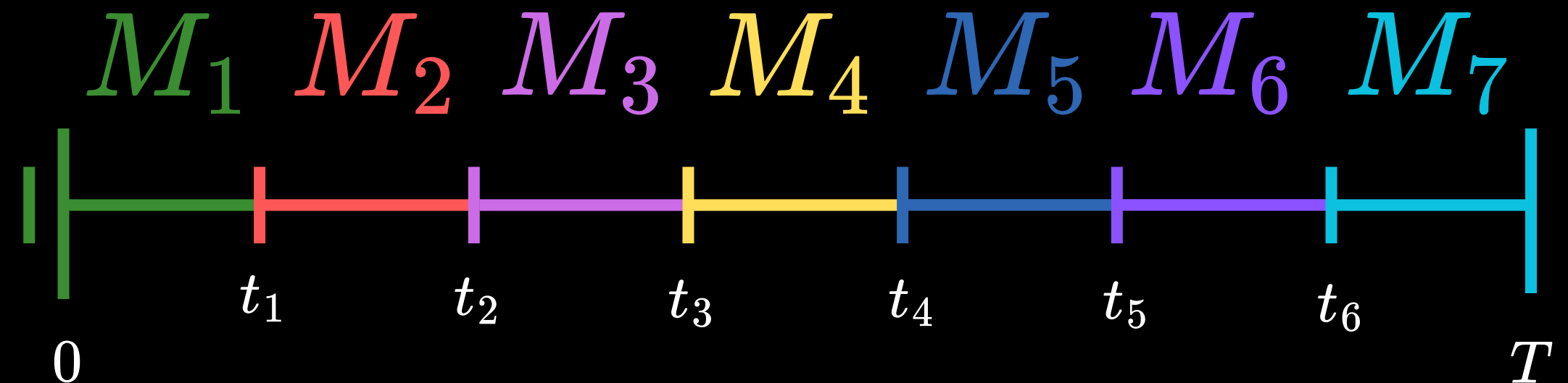


# Non-stationary Temporal Models

STATIONARY MODEL ACROSS  
THE WHOLE PERIOD

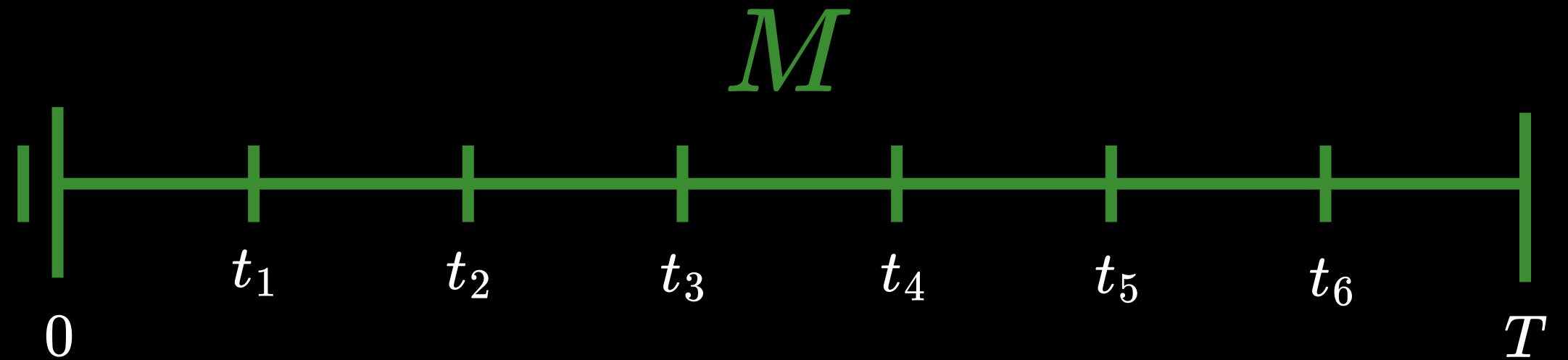


INDEEDENDENT MODELS FOR  
EACH TIME FRAME

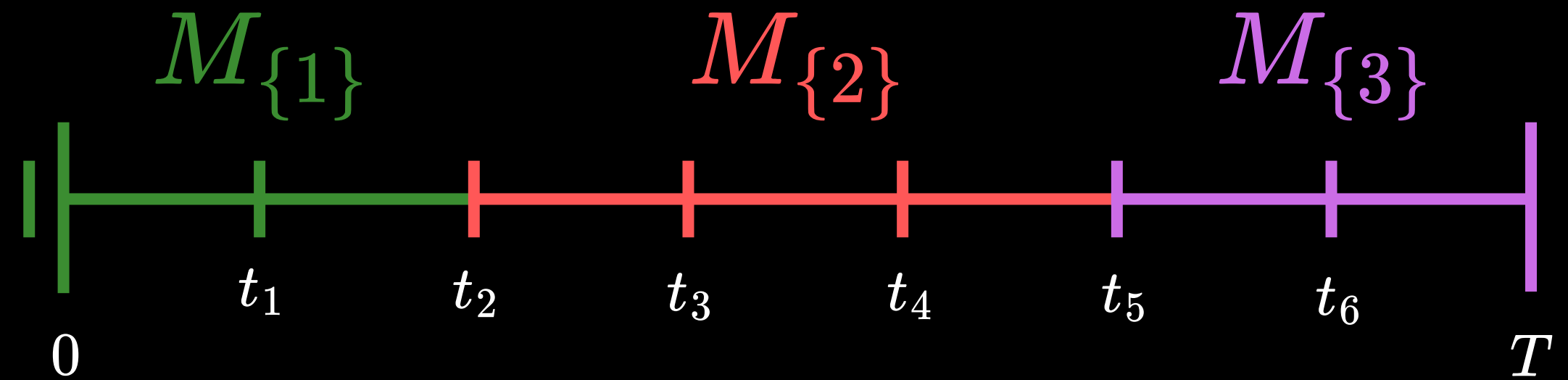


# Non-stationary Temporal Models

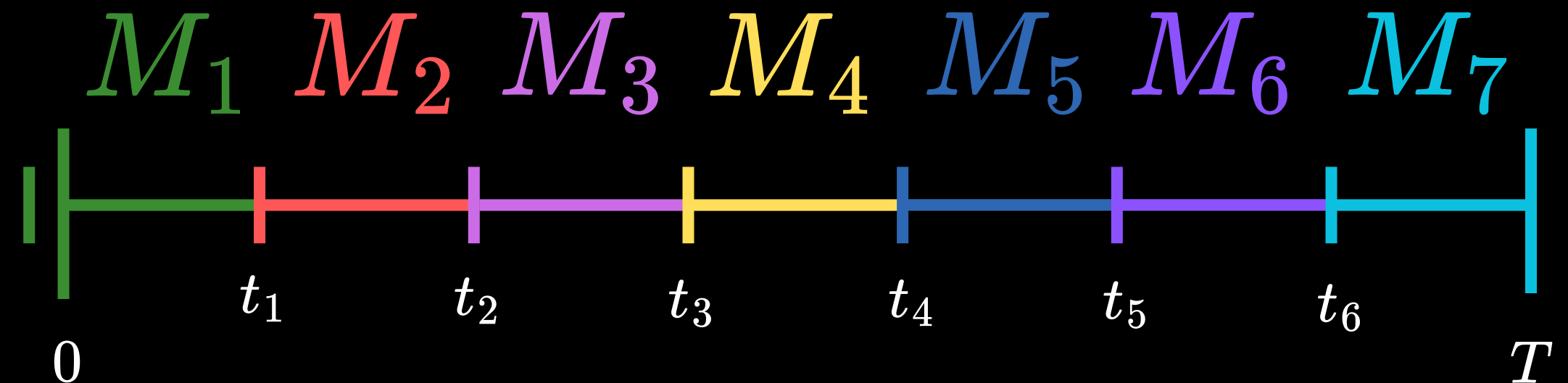
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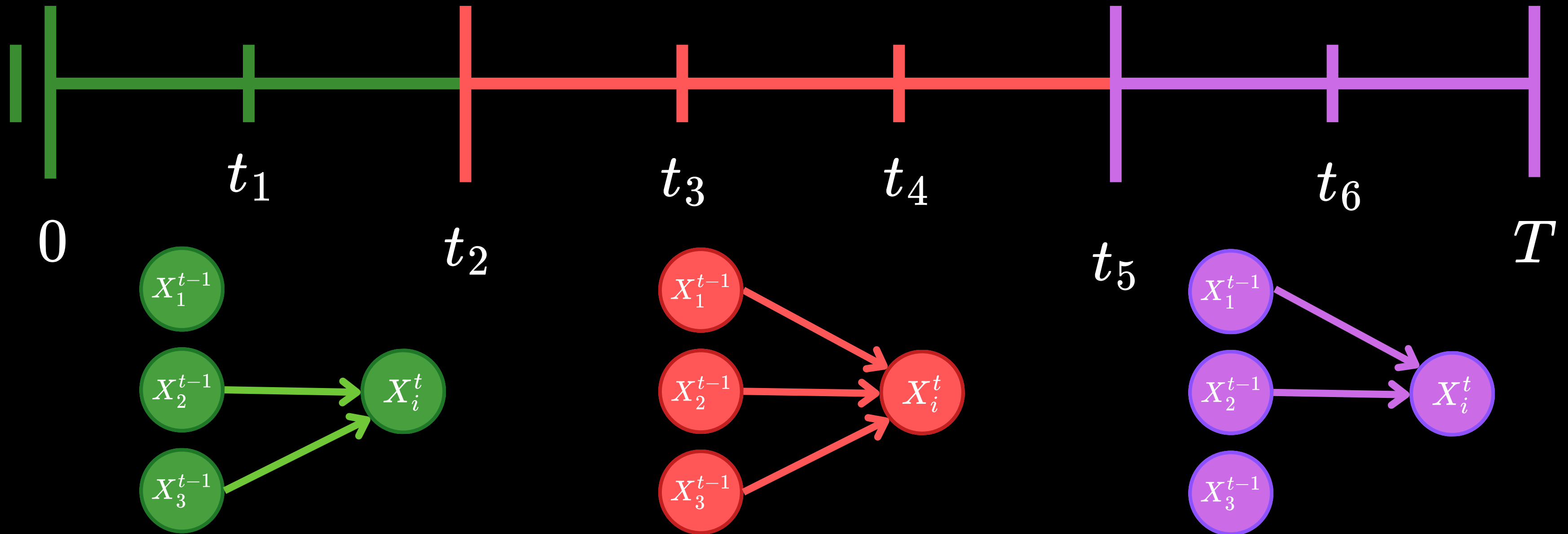
NON-STATIONARY MODEL  
with a CHANGEPOINT PROCESS



INDEEDENT MODELS FOR  
EACH TIME FRAME



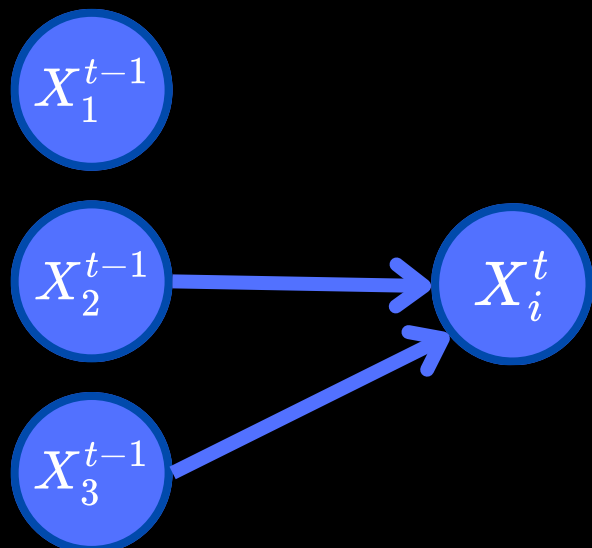
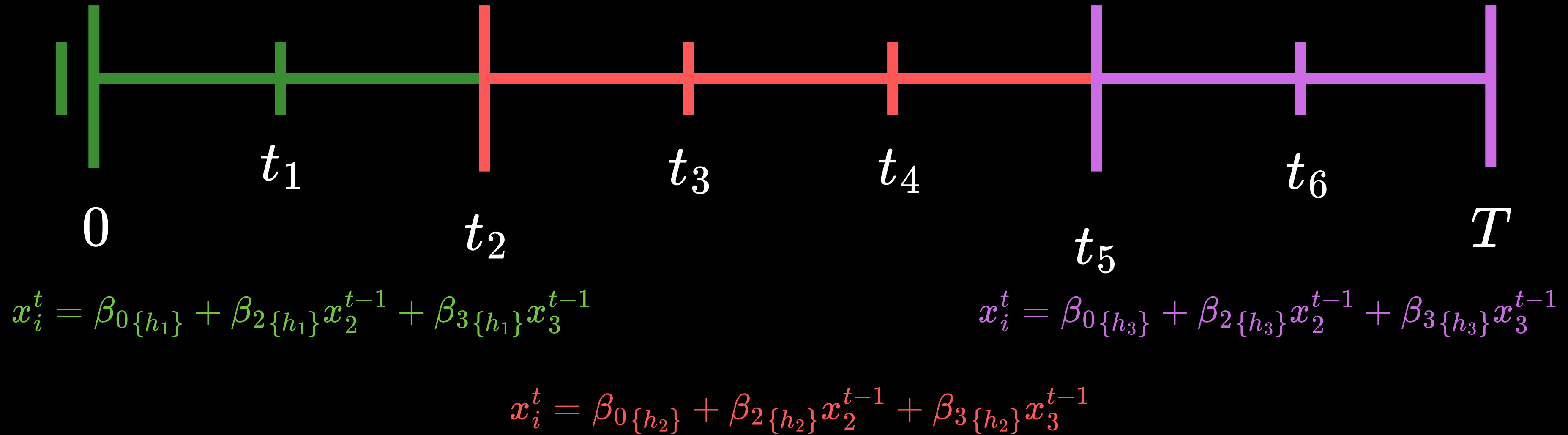
# Non-stationary and Non-homogeneous DBNs



NON-STATIONARY DBNs

Structure Changes Over Time

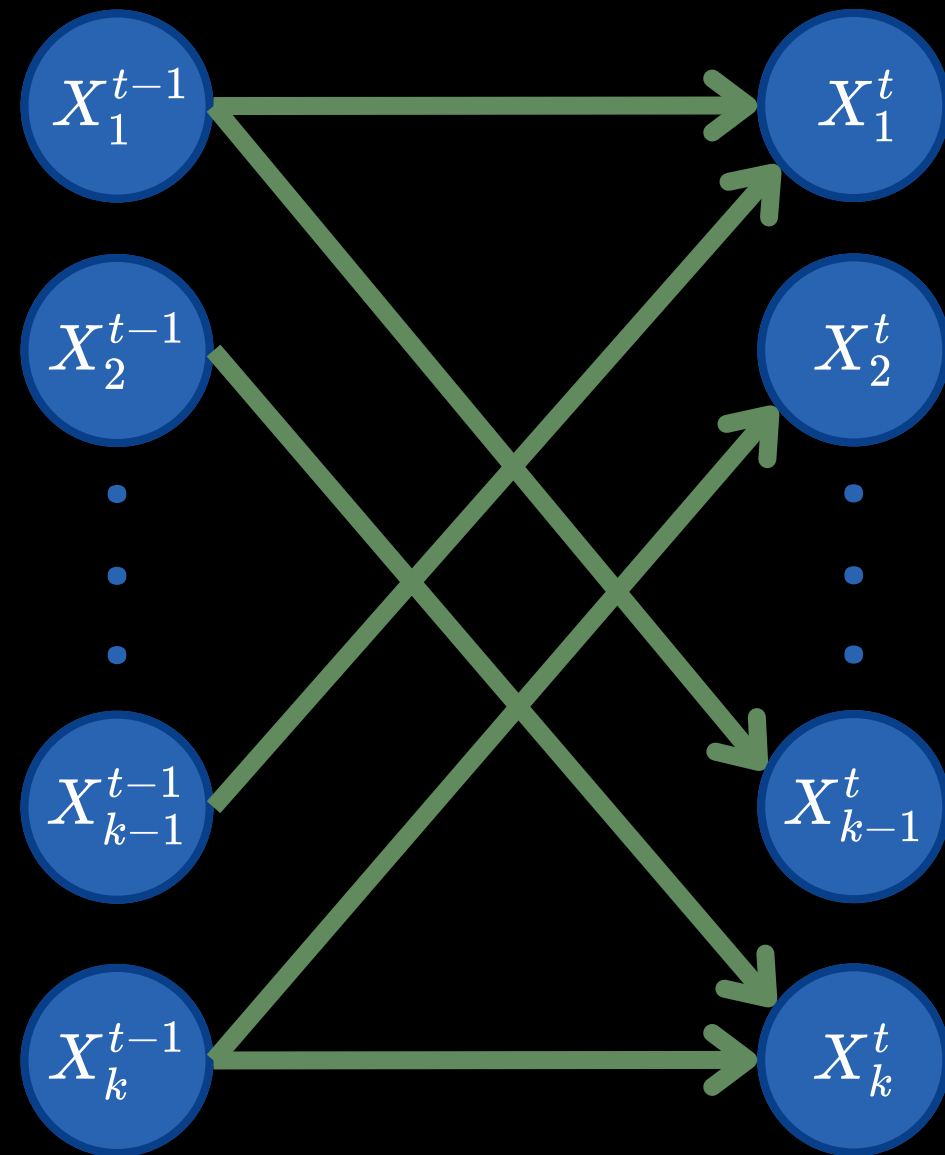
# Non-stationary and Non-homogeneous DBNs



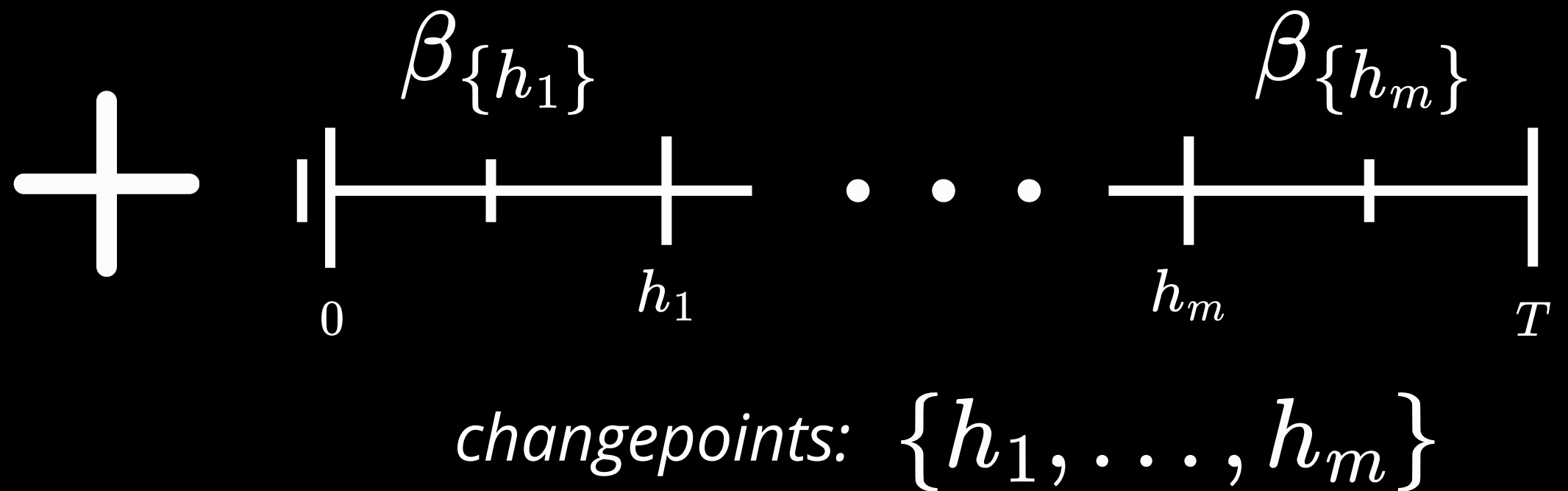
## NON-HOMOGENEOUS DBNs

Structure is Fixed - Parameters Change Over Time

# Non-homogeneous Dynamic Bayesian Networks



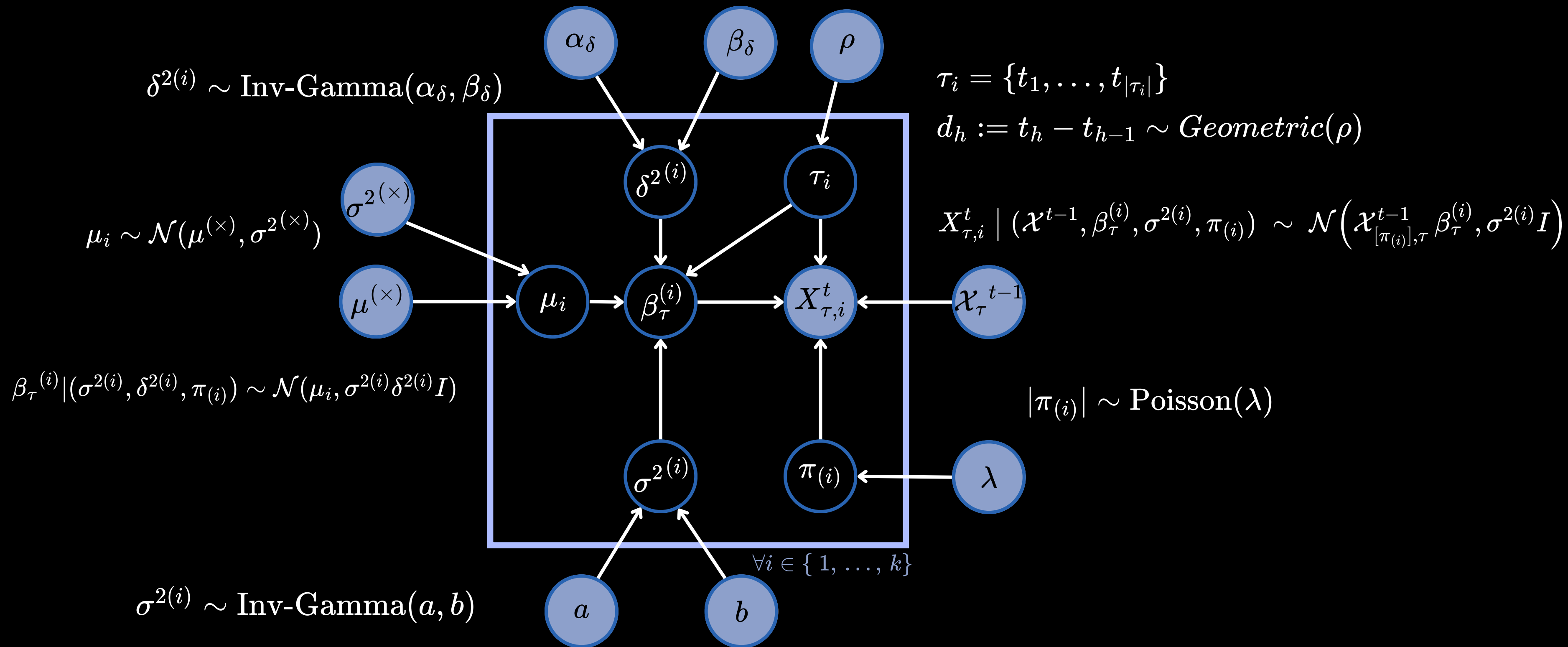
TRANSITION NETWORK



A SET OF CHANGEPOINTS

# Learning NH-DBNs from Incomplete Data

# Globally Coupled Non-Homogeneous DBNs



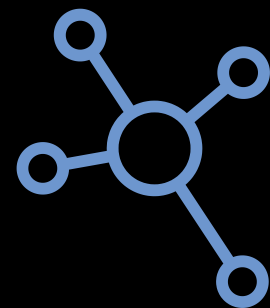
# LUME-NH Algorithm

LUME-NH is an extension of **LUME-DBN** for learning NH-DBNs from **Incomplete data**.

For each  
outcome  
variable

$\beta$   
 $\sigma$   $\delta$

PARAMETERS UPDATES: COLLAPSED GIBBS SAMPLING STEP



STRUCTURAL UPDATES: METROPOLIS-HASTING STEP



CHANGEPOINTS UPDATES: METROPOLIS-HASTING STEP



MISSING VALUES IMPUTATION: GIBBS SAMPLING STEP

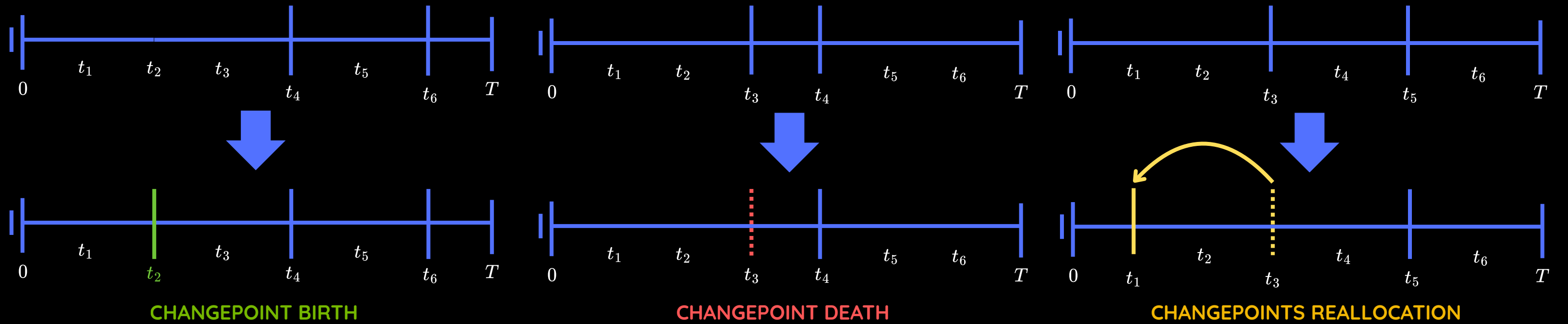
For each  
sample and  
time frame



# Changepoint Set Update

Conditional  
on the  
current  
structure  
and  
missing  
values

## Sampling a Move and Propose a new set of Changepoints



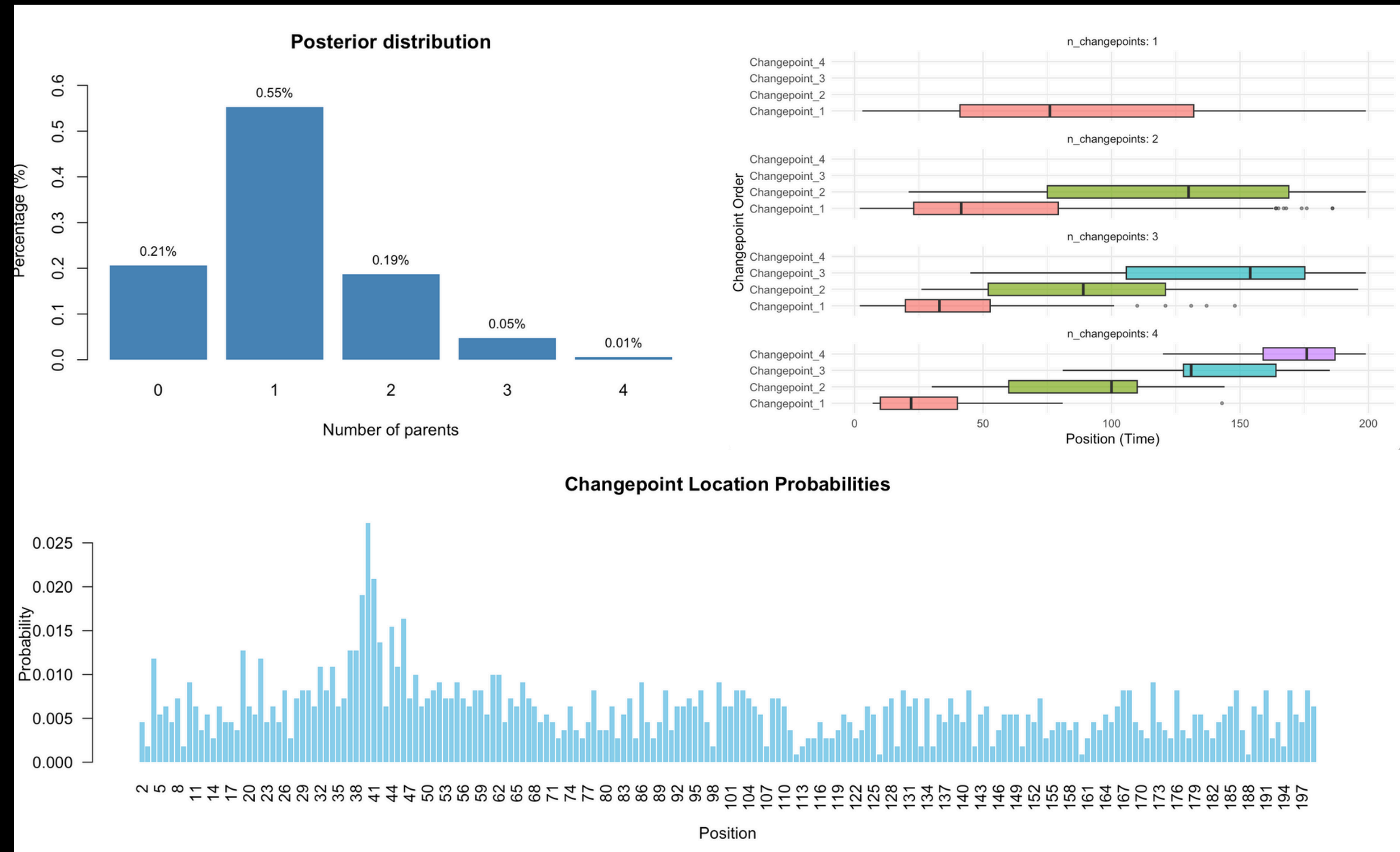
## Sampling a New Global Mean Vector

$$\tau_{\star} \sim N(\mu^{\times \times}, \Sigma^{\times \times})$$

Changepoint Set Update Probability of Acceptance for  $A > p \sim U(0, 1)$

$$A([\tau, \mu] \rightarrow [\tau_{\star}, \mu_{\star}]) = \min \left\{ 1, \frac{p(Y \mid \tau_{\star}, \mu_{\star}, \pi, \delta^2)}{p(Y \mid \tau, \mu, \pi, \delta^2)} \cdot \frac{p(\tau_{\star})}{p(\tau)} \cdot \frac{p(\mu_{\star})}{p(\mu)} \cdot \frac{p(\mu \mid \sigma^2, \delta^2, \pi, \tau, Y)}{p(\mu_{\star} \mid \sigma^2, \delta^2, \pi, \tau_{\star}, Y)} \cdot HR \right\}$$

# Posterior Distributions



# Take Home Messages

## NO MODEL FITS EVERYTHING

- In real-world settings, controlling all external factors is impracticable. Every model is therefore imperfect.
- Searching for better models matters, but acknowledging and quantifying uncertainty matters even more.

## THE APPLICATION DRIVES EVERYTHING

- A strong theoretical setting is essential, but real problems emerge in practice.
- Analyze your data. Visualize it. Let what you see challenge, and try to break your assumptions.

## EXPERT KNOWLEDGE IS NOT OPTIONAL

- Purely data-driven approaches rarely succeed, especially with limited data.
- Expert insight comes from literature, experience, and scientific reasoning. Ignoring what is already known is not innovation. It's information loss.

# Thank You