Aladynoulli: A Dynamic Model for Disease Progression

Understanding Cardiovascular Risk Through Temporal Pattern Analysis

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Outline

The Big Picture

Key Ideas

- Individual risk profiles evolve over time
- Diseases share underlying risk factors
- Genetic factors influence progression
- Time-varying disease relationships

Clinical Relevance

- Personalized risk trajectories
- Natural disease progression
- Multiple disease interactions
- Treatment planning implications

Individual Risk Profiles (λ)

Individual-Specific Signature Trajectories

For each individual i, signature k, and time t:

$$\lambda_{ik}(t) \sim \mathcal{GP}(\Gamma_k^T g_i, \Sigma_k)$$

Components:

- g_i: Genetic covariates
- Γ_k: Genetic effects
- Σ_k: Temporal covariance

Clinical Meaning:

- Personal trajectories
- Genetic influence
- Smooth evolution

Signature Proportions (θ)

From Scores to Proportions

Via softmax transformation:

$$\theta_{ik}(t) = \frac{\exp(\lambda_{ik}(t))}{\sum_{j=1}^{K} \exp(\lambda_{ij}(t))}$$

Properties:

- $\theta_{ik}(t) \in (0, 1)$
- $\sum_k \theta_{ik}(t) = 1$
- Smooth changes

Interpretation:

- Relative risk weights
- Competing factors
- Dynamic profiles

Disease Signature Loadings (ϕ)

Disease-Signature Relationships

For each disease d and signature k:

$$\phi_{kd}(t) \sim \mathcal{GP}(\mu_d, \Omega_k)$$

Components:

- μ_d: Base disease risk
- Ω_k: Signature covariance

Clinical Meaning:

- Signature-disease links
- Disease patterns
- Time variation

Disease Probabilities (π)

Individual Disease Risk

Probability for individual i, disease d, at time t:

$$\pi_{id}(t) = \sum_{k=1}^{K} \theta_{ik}(t) \cdot \text{sigmoid}(\phi_{kd}(t))$$

Components:

- Personal risk profile
- Signature contributions
- Temporal dynamics

Clinical Use:

- Risk prediction
- Trajectory planning
- Intervention timing

Cardiovascular Risk Profiles

Three Key Risk Domains

1. **Metabolic Risk**
   - Strong diabetes link
   - Gradual vascular impact
2. **Vascular Risk**
   - Primary CAD driver
   - Early HTN effects
3. **Inflammatory Risk**
   - Accelerated progression
   - Late complications

Disease Progression Patterns

Temporal Sequence

1. **Early Stage**
   - Hypertension
   - Metabolic changes
2. **Mid Stage**
   - Type 2 Diabetes
   - Early CAD signs
3. **Late Stage**
   - Clinical CAD
   - Heart Failure

Key Advantages

Clinical Strengths:

- Personalization
- Natural progression
- Multiple diseases
- Interpretable

Statistical Power:

- Temporal smoothing
- Uncertainty measures
- Principled inference

Practical Impact

- Better risk stratification
- Informed treatment planning
- Early intervention opportunities

Next Steps

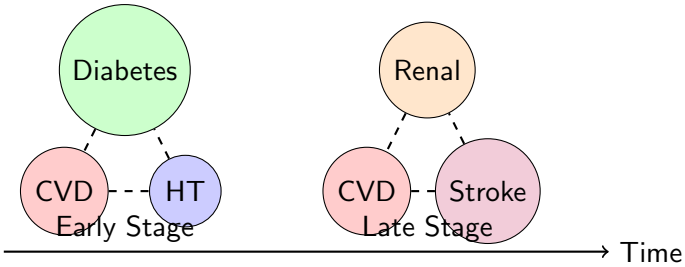
Clinical Applications

- Risk stratification tools
- Treatment optimization
- Prevention strategies

Model Extensions

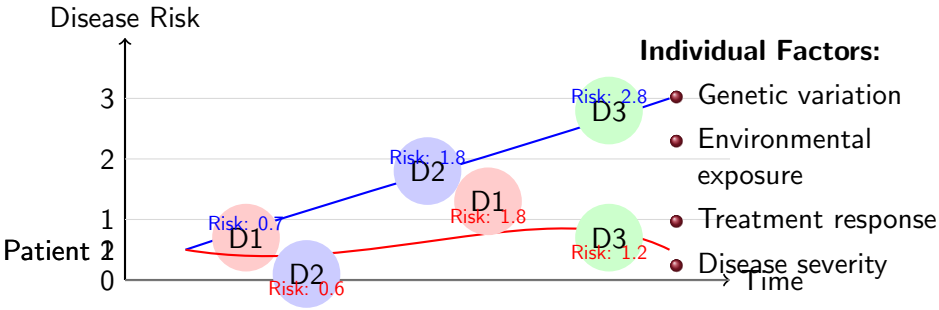
- Treatment effects
- Environmental factors
- Additional outcomes
- Real-world validation

Problem 1: Topics Need to Evolve



Standard topic models assume fixed disease relationships within topics, but disease associations change over disease progression

Problem 2: Individuals Need to Evolve



Topic models struggle with individual-specific temporal evolution and varying disease sequences