Curves to Complexity: Functional and Topological Insights into Glycemic Control in Type 1 Diabetes

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Introduction

Can daily patterns of glycemic curves in patients with type 1 diabetes reveal functional or topological signatures that can discriminate different levels of glycemic control, overcoming the limitations of traditional indicators such as HbA1c?

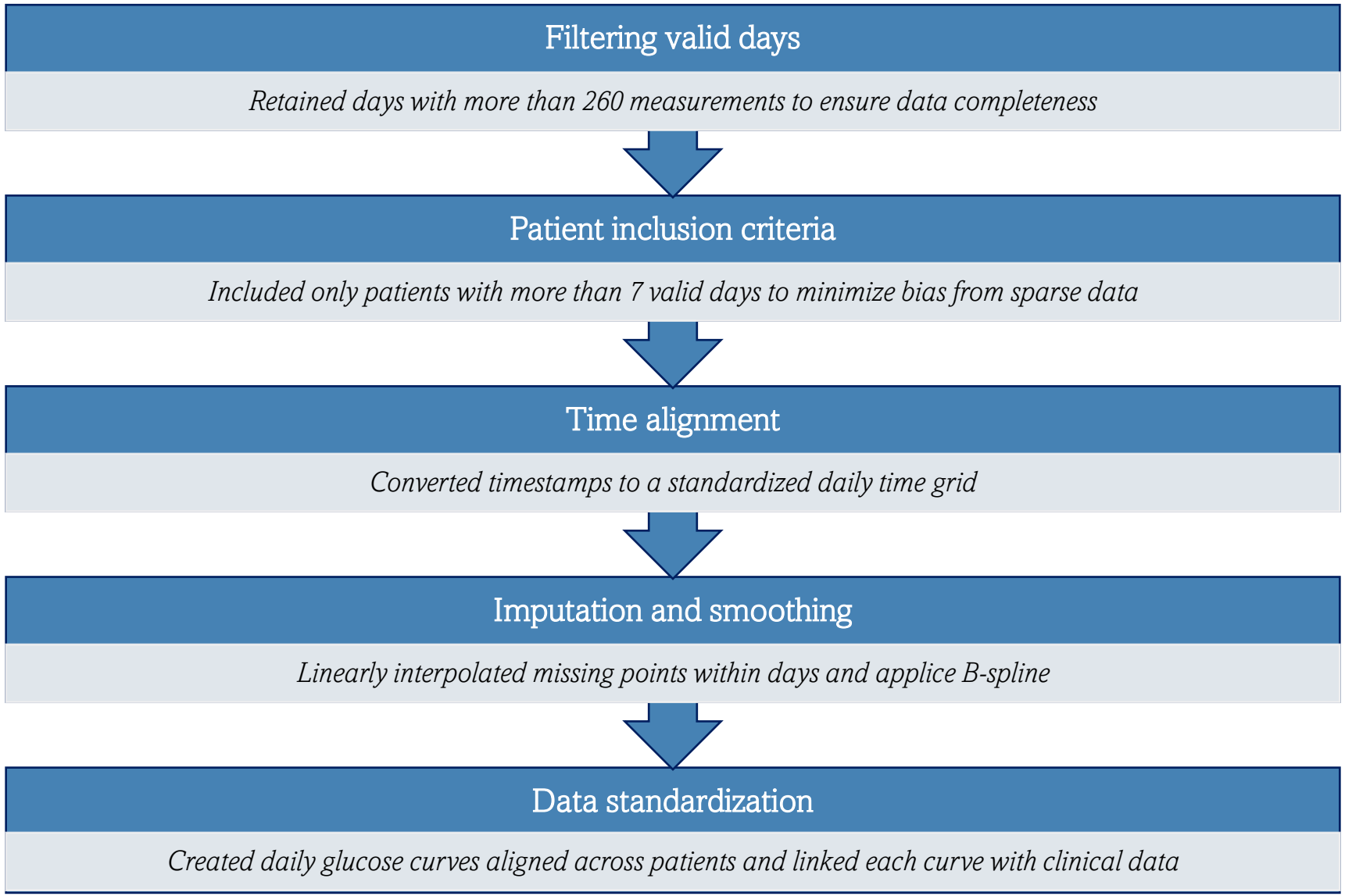
Context

- Continuous Glucose Monitoring (CGM) data enable high-resolution tracking of blood glucose fluctuations over 24-hour periods.
- Traditional summary metrics may overlook subtle yet clinically relevant glycemic patterns.
- Exploring the entire daily glucose curve using FDA and TDA may provide new insights into glycemic variability and control strategies.

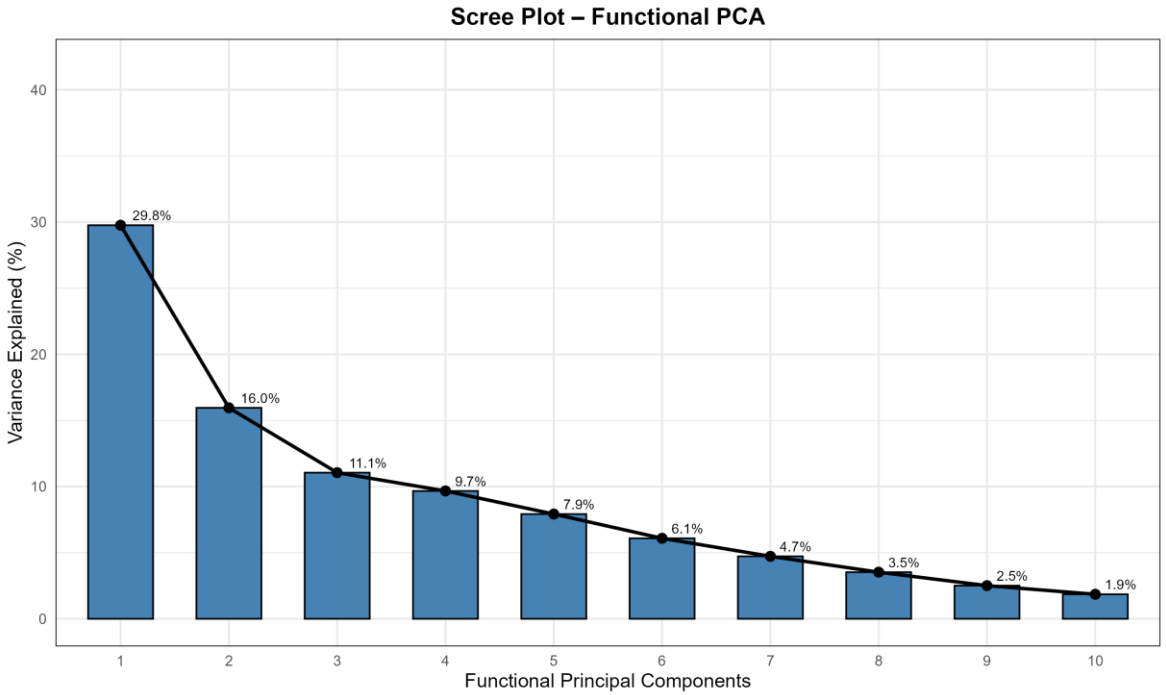
Data

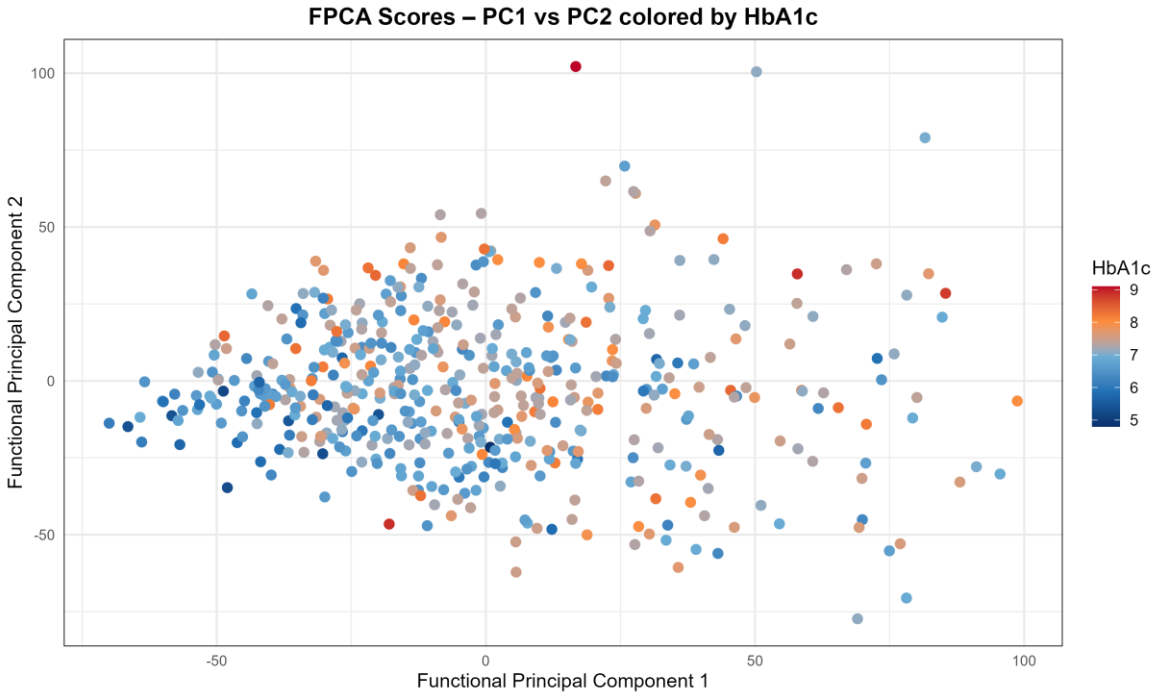
- **Sample:** 225 adults with type 1 diabetes.
- **Duration**: up to 6 months of CGM recordings per participant.
- **Measurements:** 288 glucose points per day (5-minute intervals).
- **Clinical variables**: HbA1c, frequency .of insulin boluses, fear of hypoglicemia

Data Pre-processing



Functional Principal Component Analysis

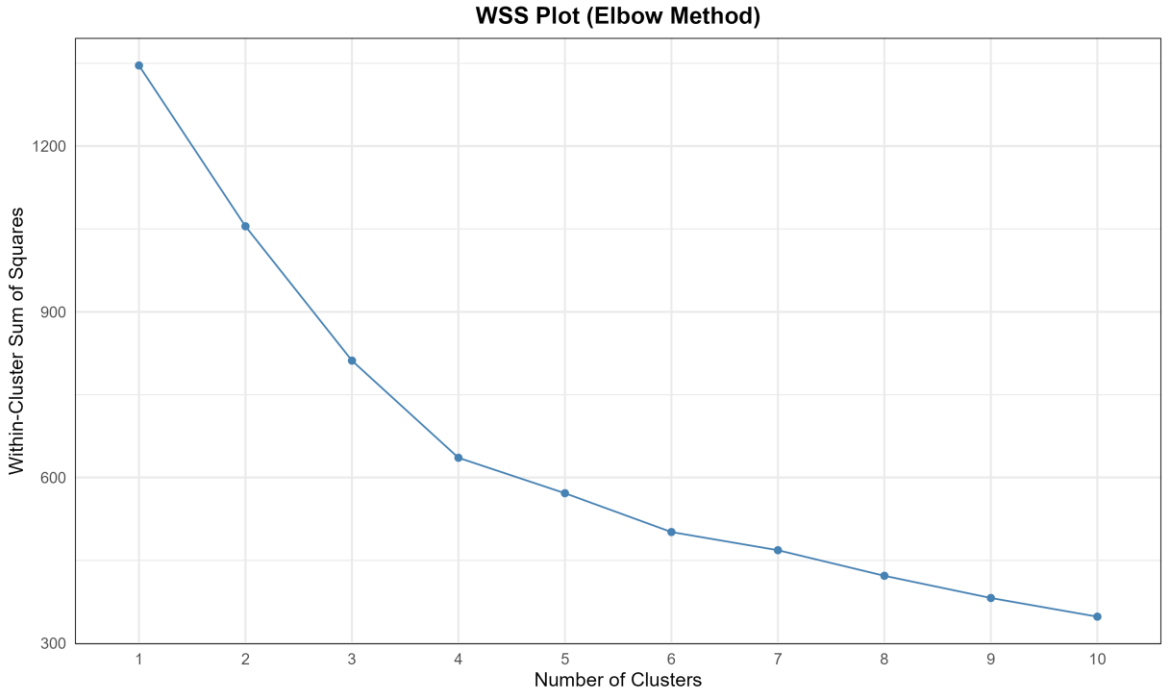


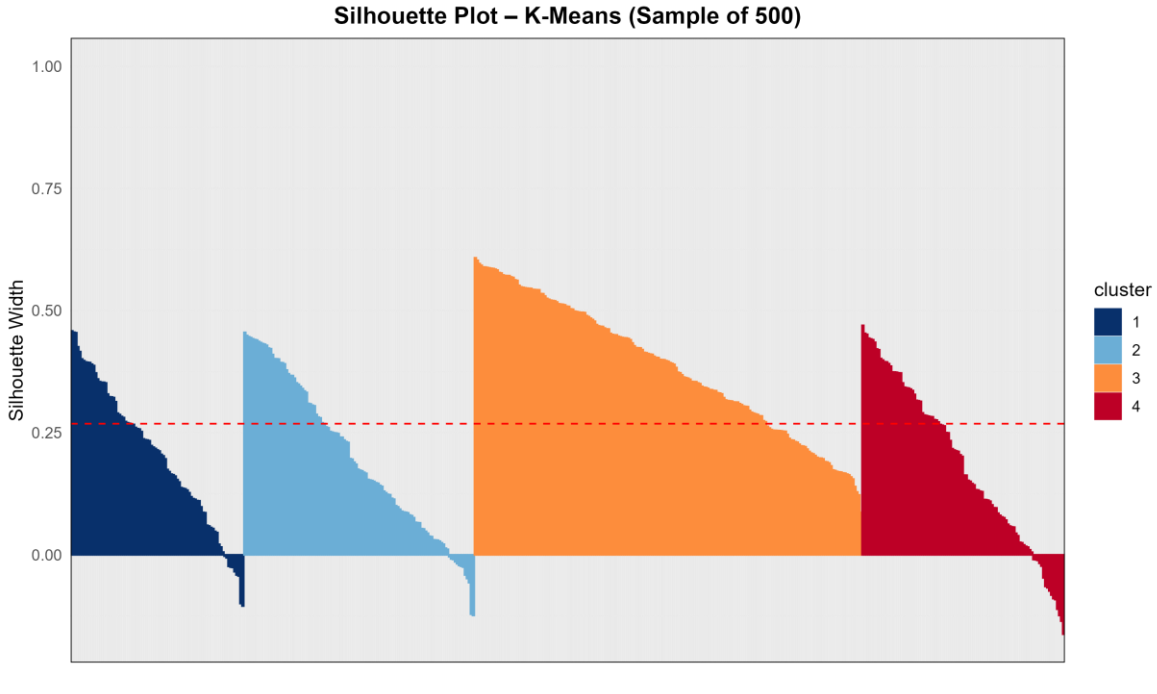


The first five harmonics (not shown here) further illustrate key patterns of variation:

- PC1 harmonic: contrasts morning vs. evening glycemic levels.
- PC2 and PC3 harmonics: capture midday peaks and instability.

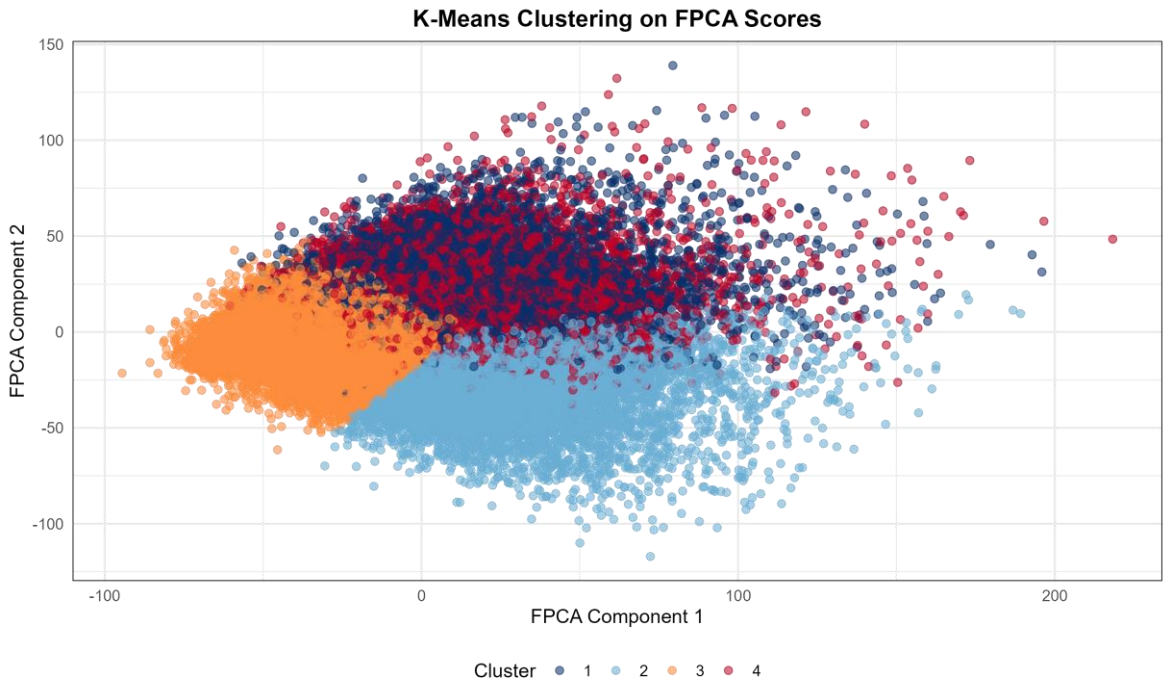
K-Means Clustering Diagnostics

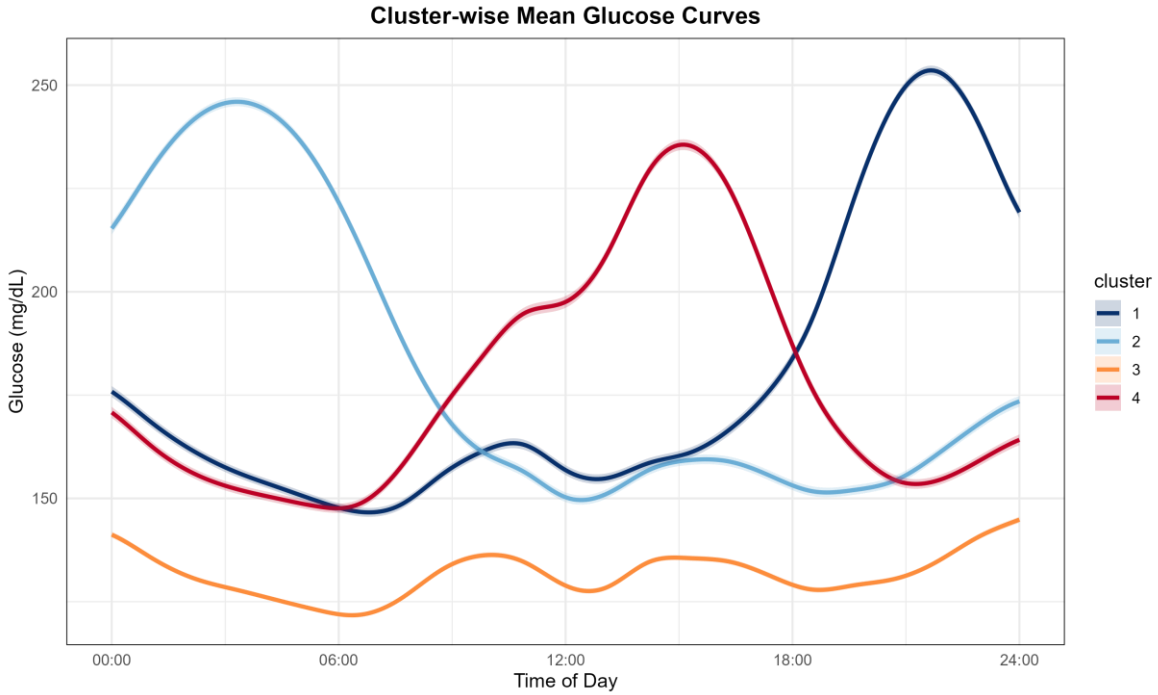




- The WSS (within-cluster sum of squares) curve shows a clear inflection at **k=4**.
  - Cluster 3: highest average silhouette (0.38) = most cohesive.
  - The overall average silhouette is <0.3 = overlap between clusters.

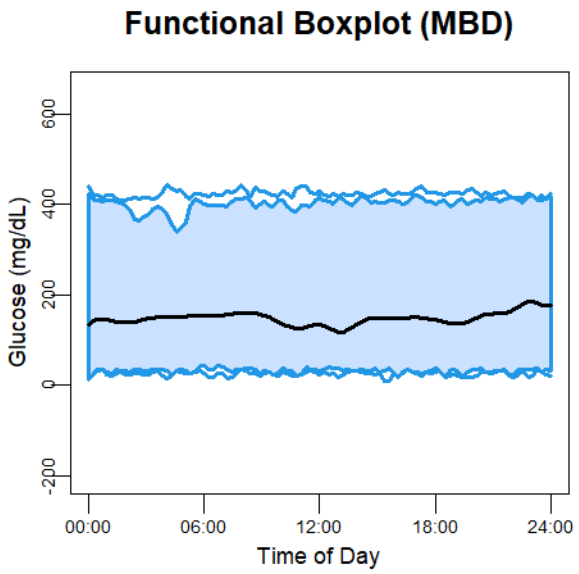
Cluster Visualization and Profiles

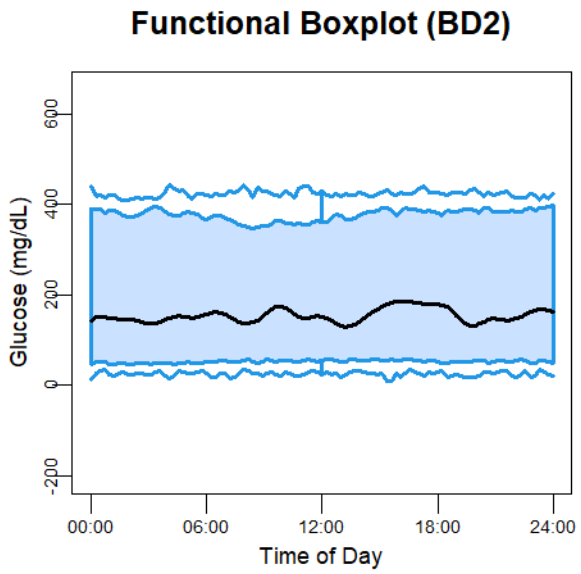


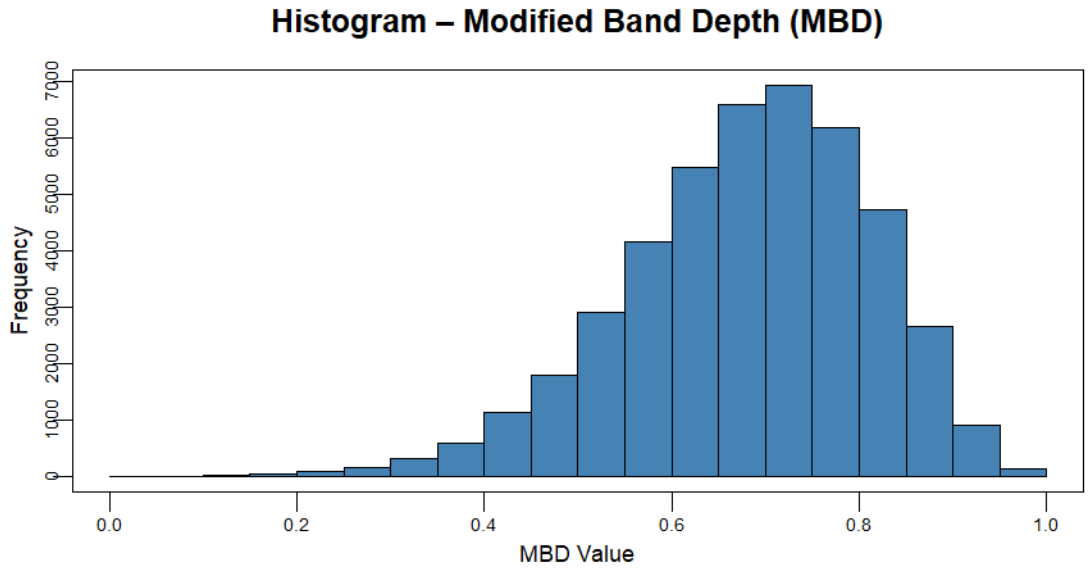


Cluster 3 appears more compact, consistent with higher silhouette scores. It has the most regular profile with well-defined meal-related peaks, associated with *lowest mean HbA1c (6.81)*

Functional Depth Analysis

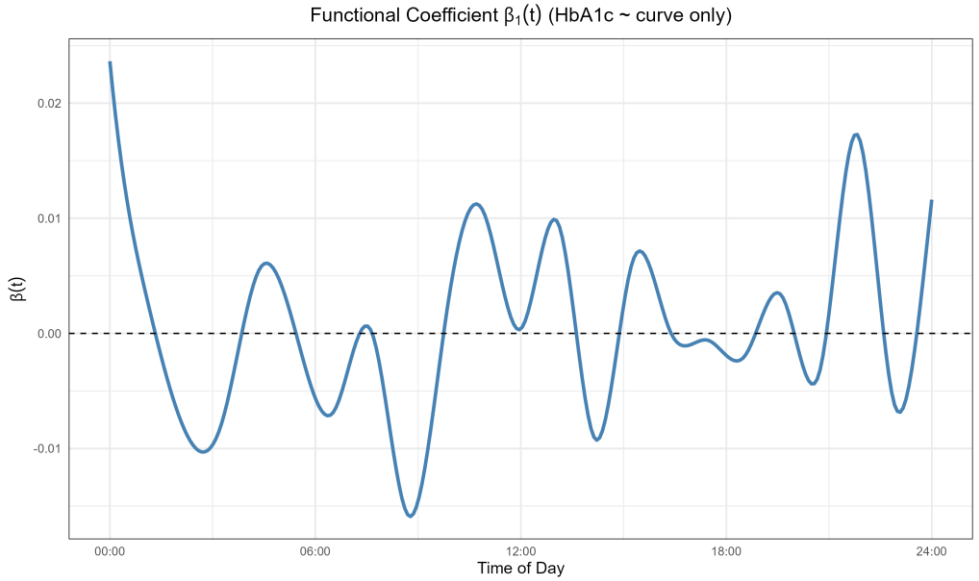


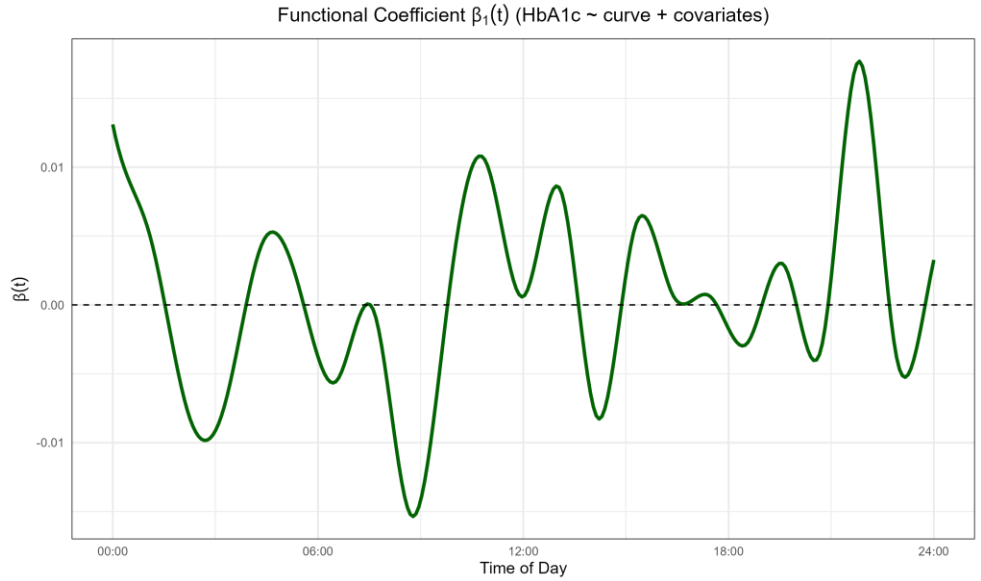


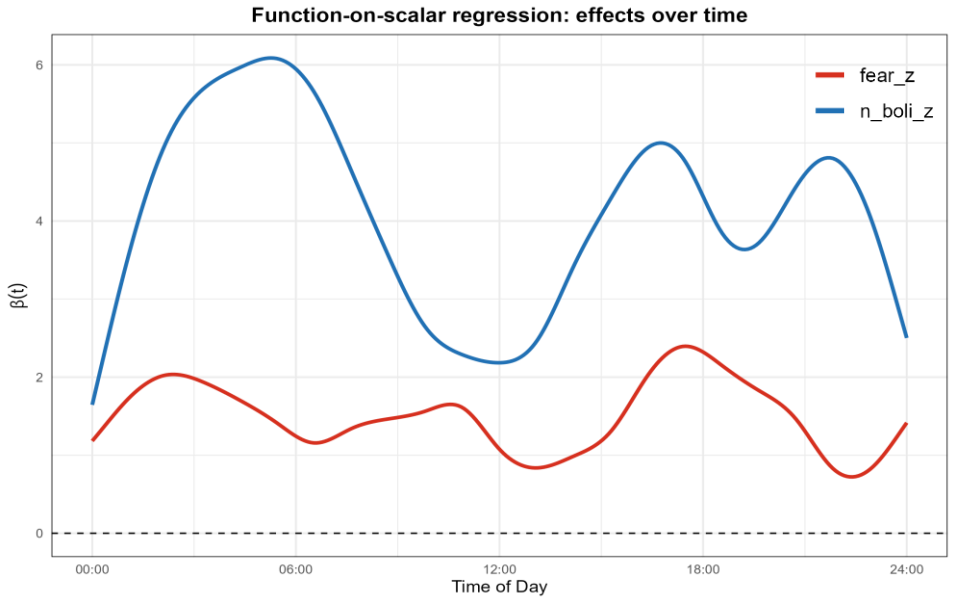


- MBD identifies overall centrality robustly, BD2 is more sensitive to local curve variations.
- Histogram confirms coexistence of a central core of stable curves and a set of more atypical profiles.
- For lower HbA1c the MBD shows more stable glycemic patterns.
- For higher HbA1c the MBD shows increased glycemic instability.

Functional Regression Models

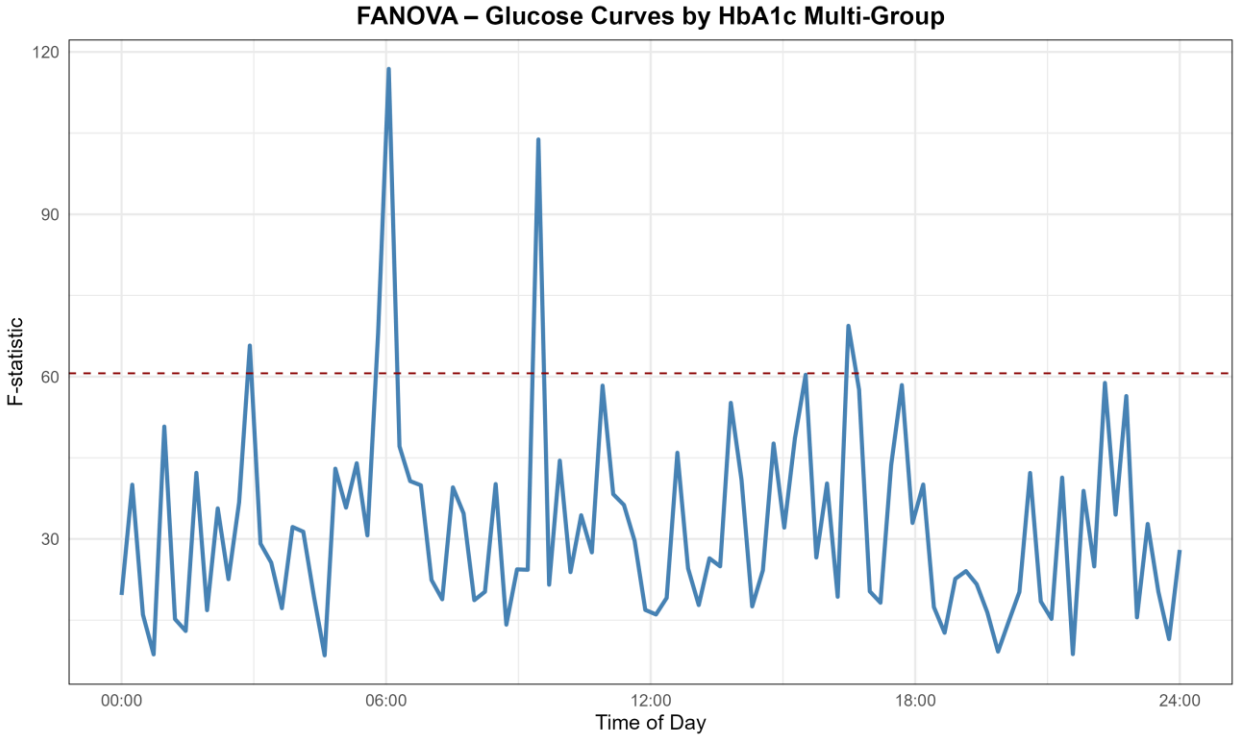


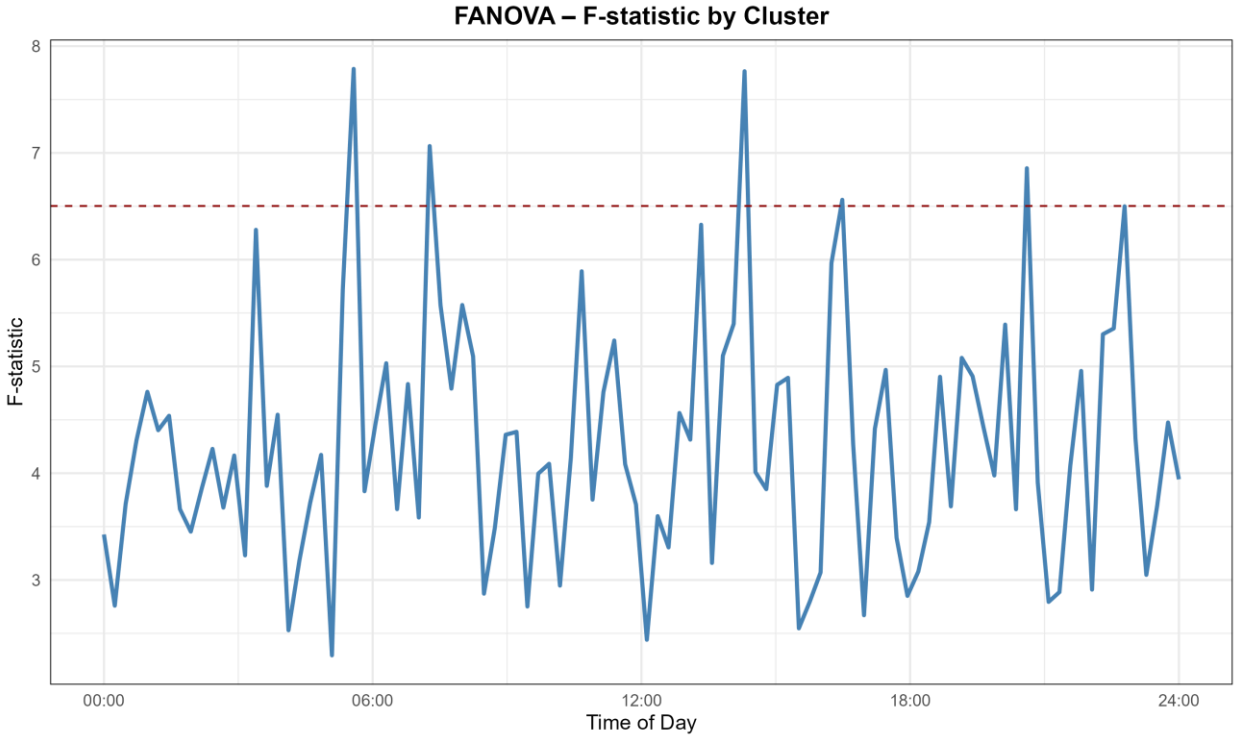




HbA1c:
has significant relationship with PC1.
Insulin boluses:
peaks match typical meal and insulin times.
Fear:
smaller, but non-negligible effects in specific periods.

Functional ANOVA Results



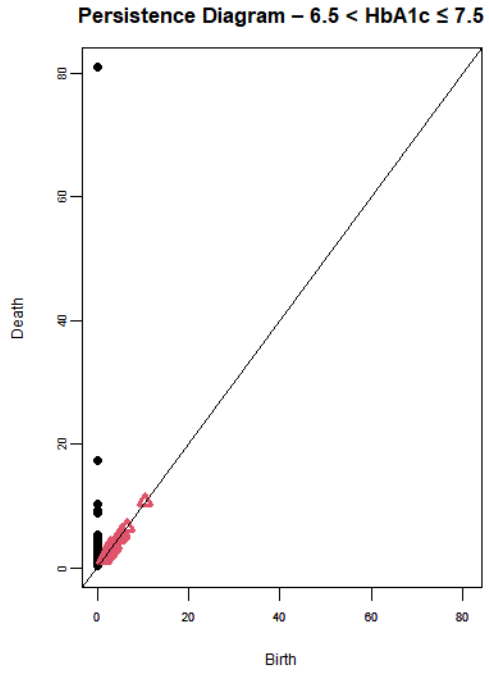


- Differences between clusters show mostly F-statistics below the significance threshold;
- No systematic differences in glycemic curves across clusters, with only occasional peaks in postprandial or night periods.

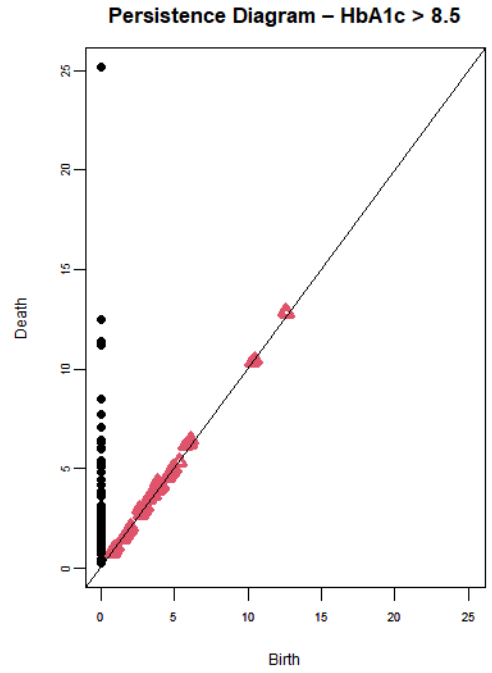
- Differences between HbA1c groups display scattered significant peaks, especially in early morning and afternoon;
- Time-specific variability related to glycemic control, but no consistent pattern across the day.

Topological Data Analysis

Persistence Diagram – HbA1c ≤ 6.5
No topological features



Persistence Diagram – 7.5 < HbA1c ≤ 8.5
No topological features



- Persistence diagrams show simple topological structures in most HbA1c groups, with little or no persistent features in well-controlled patients (HbA1c ≤ 6.5 and 7.5–8.5 groups).
- Increased topological complexity emerges in poorly controlled groups (6.5< HbA1c ≤ 7.5 and HbA1c > 8.5), reflected in more persistent connected components away from the diagonal.
- Bottleneck distance (~40.49) between intermediate and poorly controlled groups highlights significant topological differences, suggesting greater variability and fragmented glycemic patterns in patients with worse glycemic control.

Conclusions

Functional analysis showed distinct glucose patterns:
HbA1c was the main predictor, though clusters overlapped partially.

- Lower HbA1c linked to stable, central curves;
- Higher HbA1c to greater variability and instability.

- TDA revealed *simple structures* in well-controlled patients;
- but *more complex*, fragmented patterns in poorly controlled ones.

Combined FDA and TDA approaches provide quantitative tools for deeper understanding of glycemic control dynamics, with potential applications in personalized diabetes management.