



Functional Regression Methods for Densely Sampled Biomarkers in the Intensive Care Unit (ICU)

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We introduce two novel methods for expressing the association between a densely measured biomarker and an outcome, using functional regression techniques.

The first model, which we call Variable-Domain Functional Regression, extends the Generalized Functional Linear Model to the case where the subject-specific predictor functions are each observed over a different domain.

The second technique, which we have termed the Historical Cox Model, builds off of the first method by extending its context to censored survival data. In particular, the model allows one's hazard function for mortality to depend, smoothly, on their entire prior history of the time-varying biomarker, at any time. The fundamental building block of both methods is a bivariate, triangular-shaped coefficient function that depends on both the functional argument as well as the domain width.

Methods were motivated by and applied to a study of the association between daily measures of organ failure and mortality in the ICU, but are generally applicable to a large number of new studies that record continuous variables over time.