# JOINT MODELLING OF MULTIPLE LATENT PROCESSES AND A CLINICAL ENDPOINT: APPLICATION IN ALZHEIMER'S DISEASE

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Alzheimer's disease, the most frequent dementia in the elderly, is characterized by multiple progressive impairments in the brain structure and in clinical functions such as cognitive functioning and functional disability. Until recently, these components were mostly studied independently while they are fundamentally inter-related in the degradation process towards dementia.

We propose a joint model to describe the dynamics of multiple correlated latent processes which represent various domains impaired in the Alzheimer's disease. Each process is measured by one or several markers, possibly non-Gaussian. Rather than considering the associated time to dementia as in standard joint models, we assume dementia diagnosis corresponds to the passing above a covariate-specific threshold of a pathological process modelled as a combination of the domain-specific latent processes. This definition captures the clinical complexity of dementia diagnosis but also benefits from an inference via Maximum Likelihood which does not suffer from the usual complications due to numerical approximations of multivariate integrals.

The method is illustrated on large French population-based cohorts of cerebral aging which include repeated information on brain structure (hippocampus volume, cortical signature) and/or clinical manifestations (cognitive functioning, physical dependency and depressive symptoms) as well as clinical-based diagnoses of Alzheimer's disease.

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