**Appendix**

**CD4 model**

In this work the CD4 dynamic was modeled using a growth curve based on stochastic differential equations. Let yij denote the noisy measurement of CD4 and CD4ij the latent (true but not observed) value of CD4 in subject i at time j. The measurement model is defined as



With εij being the measurement errors, assumed to be independent and identically normally distributed with mean 0 and variance σ2.

The state model representing the dynamic of the latent state is based on the following stochastic differential equation relating the change in CD4 (*dCD4t*) to the current state (CD4t):



where μ represents the production of new CD4, λ the death rate of CD4-cells and Bt is a white noise representing randomness in the CD4 dynamic. Note that μ is a function of the virological status. This differential equation is also known as the mean reverted Ornstein-Uhlenbeck process and has an explicit solution [32].



where C0 = CD4(0) is the initial condition and *Asym* = μ/λ is the long term asymptote.

This model could be further improved by distinguishing within- and between-subject variation through a hierarchal (or mixed effect) formulation. The parameters *C0i*and *Asymi* for each subject are assumed to be made of a population (fixed effect) component and an additive between-subject random component, and to depend linearly on other covariates *xi*:



With **η** following a bivariate normal distribution with mean **0** and covariance matrix ∑. In this work, an interaction between the proportion of time with virological failure and the asymptotic parameter *Asym* was introduced to model the association between the immunological and virological responses. Besides, as the CD4 dynamic is expected to change abruptly after virological failure, the variance parameters of the white noise Bt was allowed to vary according to the virological state.