3.7 Pharmacokinetics; a comparison with NLME

Model description The `one-compartment open model' is commonly used in pharmacokinetics. It can be described as follows. A patient receives a dose D of some substance at time t_d. The concentration c_t at a later time point t is governed by the equation

$$c_t = \frac{D}{V} \exp\left[-\frac{Cl}{V}(t - t_d)\right]$$

where V and Cl are parameters (the so-called `Volume of concentration' and the `Clearance'). Doses given at different time points contribute additively to c_t. Pinheiro & Bates (2000, Ch. 6.4) fitted this model to a dataset using the S-Plus routine `nlme`. The linear predictor used by Pinheiro & Bates (2000, p. 300) is:

$$\begin{aligned} \log(V) &= \beta_1 + \beta_2 Wt + u_V, \\ \log(Cl) &= \beta_3 + \beta_4 Wt + u_{Cl}, \end{aligned}$$

where Wt is a continuous covariate, and $u_V \sim N(0, \sigma_V^2)$ and $u_{Cl} \sim N(0, \sigma_{Cl}^2)$ are random effects. The model specification is completed by the requirement that the observed concentration y in the patient is related to the true concentration by $y = c_t + \varepsilon$, where $\varepsilon \sim N(0, \sigma^2)$ is a measurement error term.

Results Estimates of hyper-parameters are shown in the following table:

	β_1	β_2	β_3	β_4	σ	σ_V	σ_{Cl}
ADMB-RE	-5.99	0.622	-0.471	0.532	2.72	0.171	0.227
Std. Dev	0.13	0.076	0.067	0.040	0.23	0.024	0.054
`nlme`	-5.96	0.620	-0.485	0.532	2.73	0.173	0.216

The differences between the estimates obtained with ADMB-RE and `nlme` are caused by the fact that the two methods use different approximations of the likelihood function. ADMB-RE uses the Laplace approximation, while the method used by `nlme` is described in Pinheiro & Bates (2000, Ch. 7).

The time taken to fit the model by ADMB-RE was 17 seconds, while the computation time for `nlme` (under S-Plus 6.1) was 7 seconds.