

Use of dynamical models for treatment optimization in HIV infected patients

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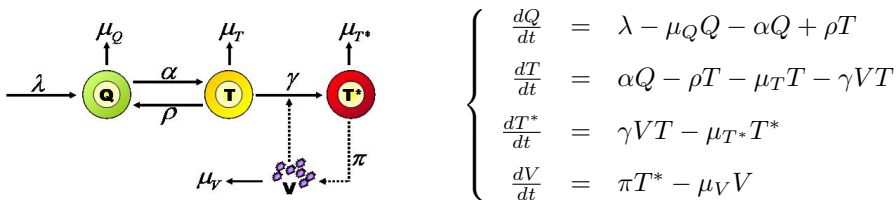
Invited guests : V. De Gruttola

November, 15th 2013



HIV mechanistic model

Target cells model [Guedj et al. 2007 ; Drylewicz et al. 2010 ; Prague et al. 2012]



For other modeling :

Journal : [Advanced Drug delivery reviews](#)

Details : 65(7) :954-965 (June 2013)

Title : Dynamical models of biomarkers and clinical progression for personalized medicine : the HIV context.

Authors : [Prague M.](#), [Commenges D.](#) and [Thiébaud R.](#)

Statistical model

Mixed Effects model on parameters (γ , μ_{T^*} and λ) :

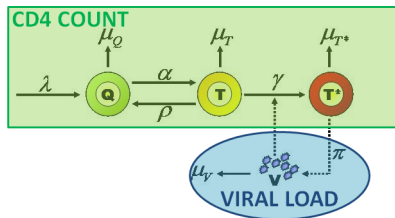
- Fixed effects : Pharmacokinetics/Pharmacodynamics/Covariates. . .
- Random effects : Inter-individual variability

$$\tilde{\xi}^i = \log(\alpha^i, \lambda^i, \dots, \gamma_0^i, \mu_V^i)$$

$$\tilde{\xi}_l^i = \underbrace{\phi_l + d_l^i(t)\beta_l}_{\text{Fixed effects}} + \underbrace{u_l^i}_{\text{Random effects}}$$

$$u^i \sim \mathcal{N}(0, I_q)$$

Observational Model



Viral Load : $Y_{ij1} = \log_{10}(V) + \epsilon_{ij1}$

Total CD4 count : $Y_{ij2} = (Q + T + T^*)^{0.25} + \epsilon_{ij2}$

$$\epsilon_{ijm} \sim \mathcal{N}(0, \sigma_m^2)$$

NIMROD : Optimization algorithm

Parameters of interest :

$$\theta = \left[(\phi_l)_{l=1\dots n_b}, (\beta_l)_{l=1\dots n_e}, (\omega_l)_{l=1\dots q}, (\sigma_l)_{l=1\dots M} \right]$$

Estimator tool :

Journal : Computer Methods and Programs in Biomedicine

Details : 111(2) :447-458 (Aug. 2013)

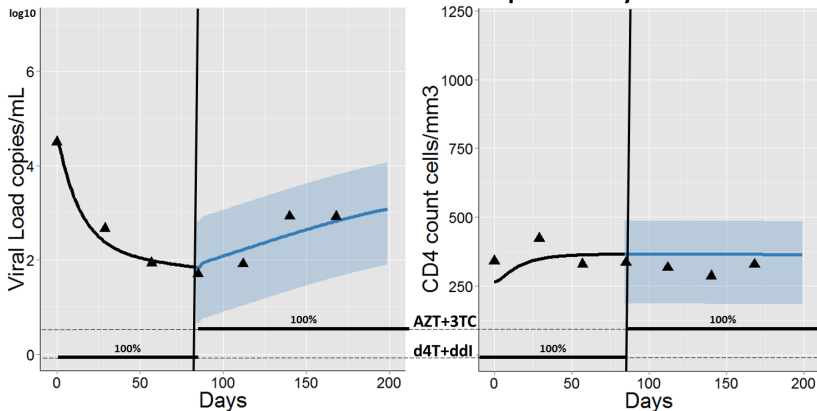
Title : NIMROD : A Program for Inference via Normal Approximation of the Posterior in Models with Random effects based on Ordinary Differential Equations.

Authors : [Prague M.](#), Commenges D., Guedj J., Drylewicz J. and Thiébaud R.

- Penalized likelihood maximization,
- Normal approximation of the posterior,
- Comparison with FOCE and MCMC,
- Software Distribution with parallel computing.

Prediction abilities on ALBI clinical trial

Predictions of biomarkers with 95% predictivity intervals



We are able to predict the Viral load and CD4 count trajectories (here, a rebound for viral load) for patient who [changed treatment molecule](#).

Adaptive treatment strategy : what's next ?

Journal : Biometrics

Details : 68(3) :902-911 (sept. 2012)

Title : Treatment monitoring of HIV infected patients based on mechanistic models.

Authors : Prague M., Commenges D., Drylewicz J. et Thiébaud R.

