

# Defining NLME Models in PuMaS

```
1 nlme_model = @model begin
2   @param begin
3     θ ∈ VectorDomain(3,init=[3.24467E+01, 8.72879E-02, 1.49072E+00])
4     Ω ∈ PSDDomain(init=Matrix{Float64}([ 1.93973E-02  1.20854E-02  5.69131E-02
5                                           1.20854E-02  2.02375E-02 -6.47803E-03
6                                           5.69131E-02 -6.47803E-03  4.34671E-01]))
7     Σ ∈ PDiagDomain(init=[1.70385E-02, 8.28498E-02])
8   end
9
10  @random begin
11    η ~ MvNormal(Ω)
12  end
13
14  @pre begin
15    V = θ[1] * exp(η[1])
16    Ke = θ[2] * exp(η[2])
17    Ka = θ[3] * exp(η[3])
18    CL = Ke * V
19  end
20
21  @vars begin
22    conc = Central / V
23  end
24
25  @dynamics begin
26    Gut' = -Ka*Gut
27    Central' = Ka*Gut - Ke*Central
28  end
29
30  @derived begin
31    dv ~ @. Normal(conc,sqrt(conc^2 *Σ.diag[1] + Σ.diag[end])+eps())
32  end
33 end
```

## @param: Model parameters (Population averages)

```
1 @param begin
2      $\theta_1$   $\in$  RealDomain(lower=0.1, init=2.77, upper=5.0)
3      $\theta_2$   $\in$  RealDomain(lower=0.008, init=0.0781, upper=0.5)
4      $\theta_3$   $\in$  RealDomain(lower=0.004, init=0.0363, upper=0.9)
5      $\Omega$   $\in$  PSDDomain(2, init=diag([5.55, 0.515]))
6      $\sigma_2$   $\in$  RealDomain(lower=0.0, init=0.388)
7 end
```

This specifies the parameters of the model, and their domains:

- RealDomain: real values (possibly subject to upper/lower bounds)
- VectorDomain: vector of real values
- PSDDomain: symmetric positive-definite matrices (e.g. for covariance matrices)
- PDiagDomain: positive-valued diagonal matrices

## @random: Random effects (Individual differences)

```
1 @random begin
2      $\eta$   $\sim$  MvNormal( $\Omega$ )
3 end
```

Specifies the random effects, dependent on parameters. The random effects are defined by a distribution from Distributions.jl.