Accelerating Access to Life-Saving Treatments to Patients

pumas AI

Augment Workflow

DeepPumas Workshop
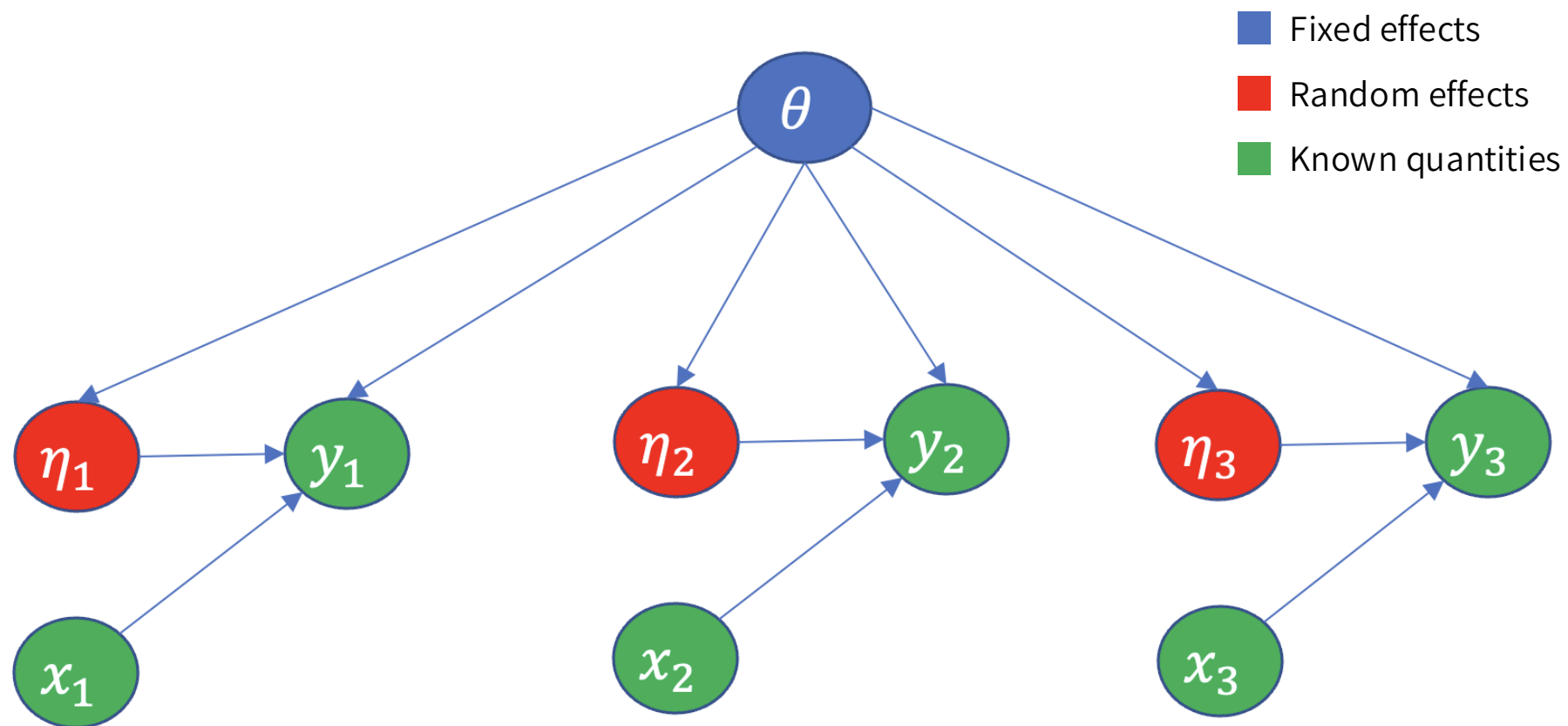
Prepared by: Mohamed Tarek

Pumas-AI Inc

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Classical NLME Model

Pumas Model

θ

$\eta_i \mid \theta$

x_i

$y_i \mid \theta, \eta_i, x_i$

```julia
@model begin
  @param begin
    θ ∈ VectorDomain(4, lower = zeros(4))
    Ω ∈ PSDDomain(2)
    Σ ∈ RealDomain(lower = 0.0)
    a ∈ RealDomain(lower = 0.0, upper = 1.0)
  end
  @random begin
    η ~ MvNormal(Ω)
  end
  @covariates sex wt etn
  @pre begin
    θ1 := θ[1]
    Ka = θ1
    CL = θ[2] * ((wt / 70)^0.75) * (θ[4]^sex) *
      exp(η[1])
    Vc = θ[3] * exp(η[2])
  end
  @dynamics begin
    Depot' = -Ka * Depot
    Central' = Ka * Depot - (CL / Vc) * Central
    Res' = Depot - Central
  end
  @derived begin
    conc = @. Central / Vc
    dv ~ @. Normal(conc, conc * Σ)
    T_max = maximum(t)
  end
  @observed begin
    obs_cmax = maximum(dv)
  end
end
```
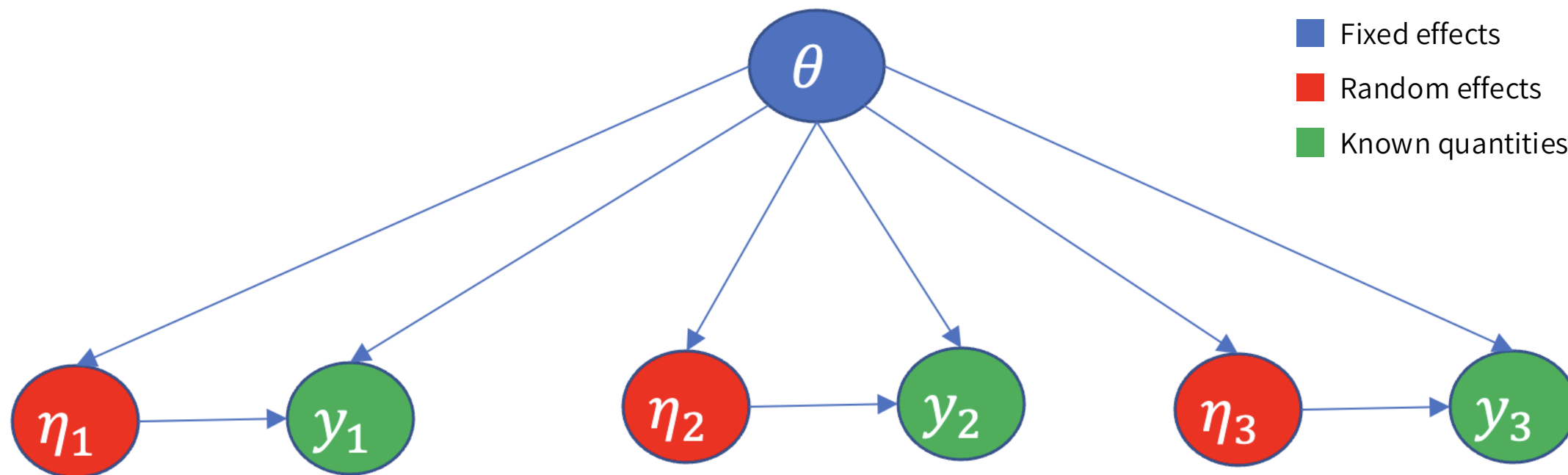
Covariate Free Model
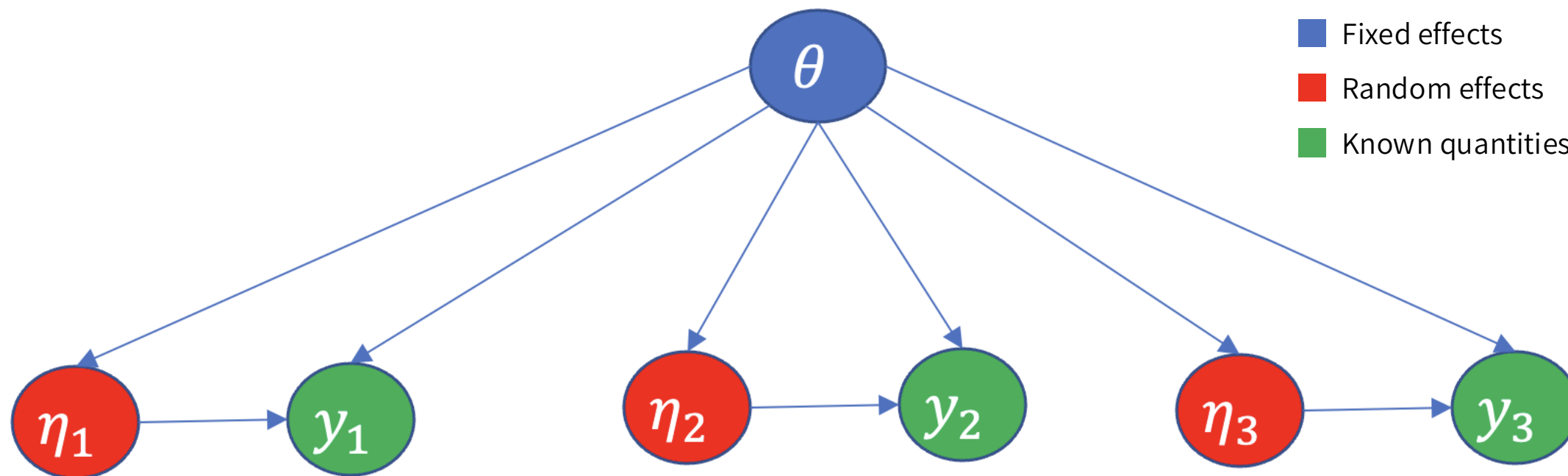
The NLME UDE models we have seen are covariate free!
They cannot exploit known heterogeneity in the patients to give better predictions!
In absence of observed data, their best prediction is independent of the individual under consideration.
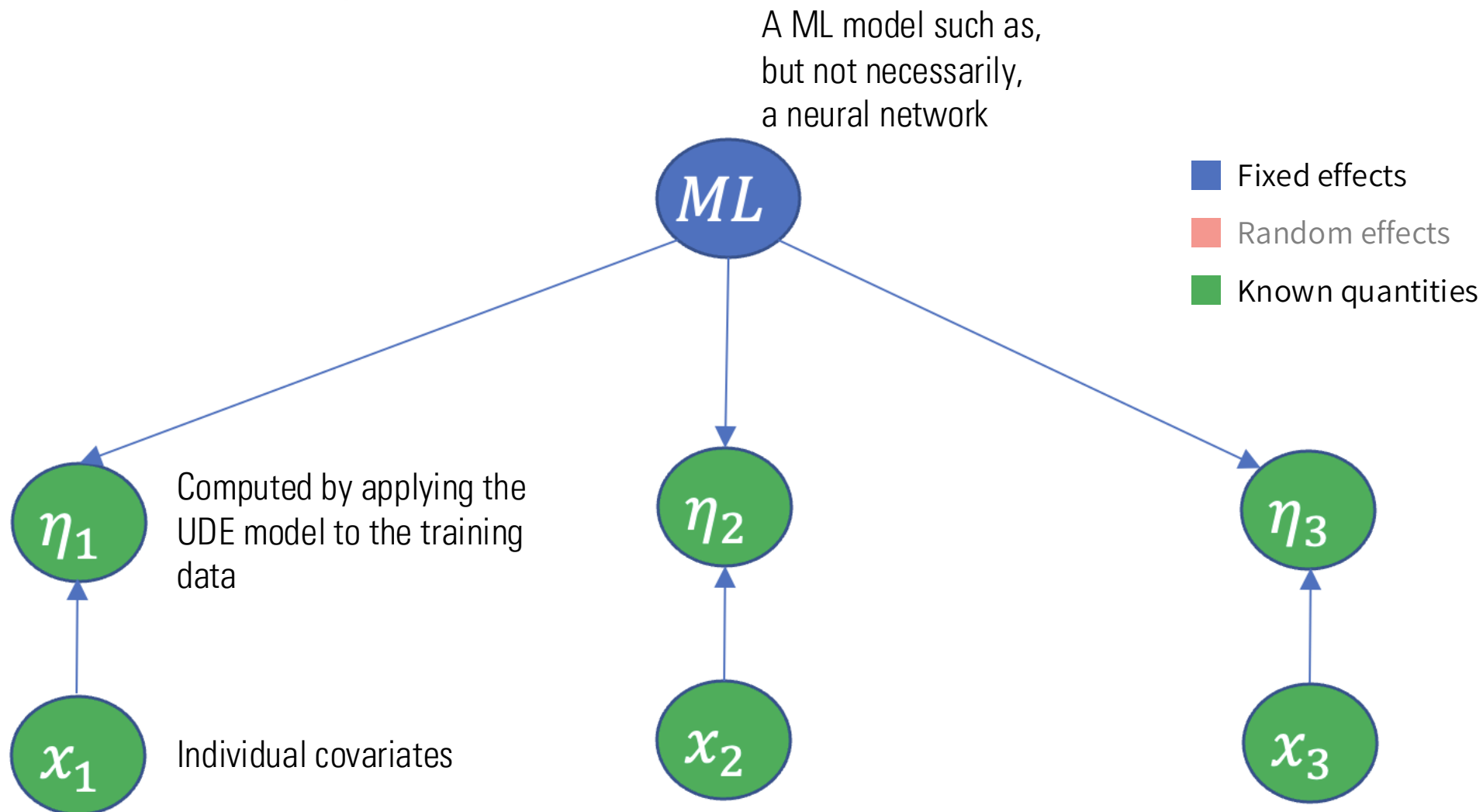This is far from ideal.

Covariate Free Model

Fixed effects
Random effects
Known quantities

However, if we could find a function mapping the covariates to the random effects of the UDE model, we could give better predictions even in absence of observed data.
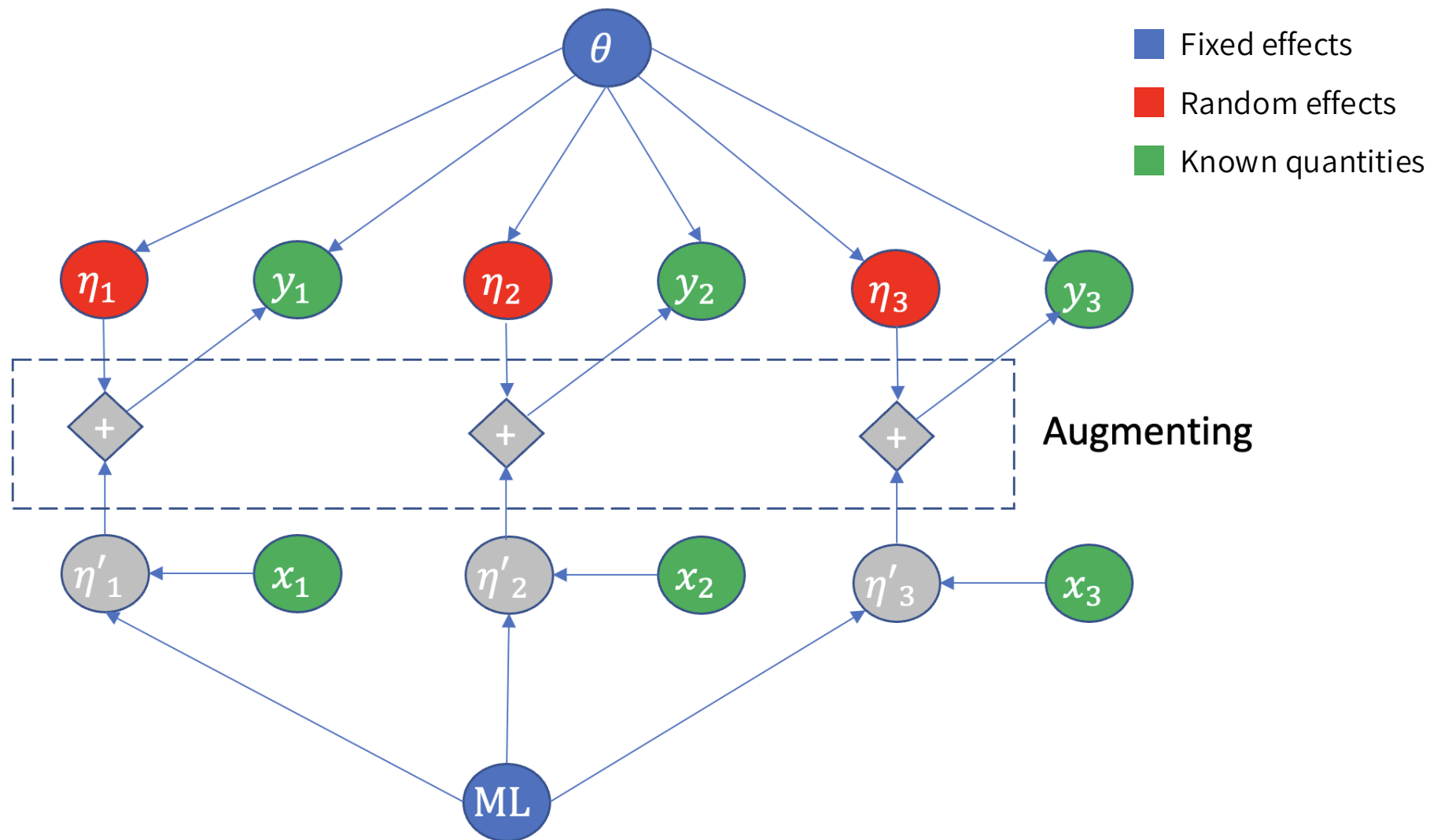
Supervised Learning

A ML model such as, but not necessarily, a neural network

Fixed effects
Random effects
Known quantities

ML

η_1 — Computed by applying the UDE model to the training data

η_2

η_3

x_1 — Individual covariates

x_2

x_3

Augmented Model

In short

1. Fit an NLME model to describe individual time courses using random effects

2. Extract an approximation of the posterior distribution of the random effects for each subject in the training data.

3. Fit a machine learning model to predict these posterior distributions from covariates

4. Augment the original NLME model with the machine learning prediction of the random effect value.