The following information relates to the manuscript:

Dynamic modeling of practice effects across the healthy aging-Alzheimer's disease continuum

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Following the **ctsem** package, we typically consider the continuous time equations portrayed by the multivariate stochastic differential equation. More details on the modelling setup can be found at Driver et al., 2017; Driver and Voelkle, 2021. For demonstrating the basic model structure for an typical example, here we consider the sensitivity model considering age as the time independent predictor. The subject level model can be described as follows:

Subject parameter distribution:

$$
\underbrace{\begin{bmatrix} \text{pracEffect}_i \\ \text{mm\_Trial\_1}_i \\ \text{mm\_Trial\_2}_i \\ \text{mm\_Trial\_3}_i \\ \text{mm\_Trial\_4}_i \\ \text{selfFeedback\_practice}_i \\ \text{selfFeedback}_i \\ \text{diff\_t1}_i \\ \text{diff\_t2\_t1}_i \\ \text{diff\_t2}_i \\ \text{diff\_t3\_t1}_i \\ \text{diff\_t3\_t2}_i \\ \text{diff\_t3}_i \\ \text{diff\_t4\_t1}_i \\ \text{diff\_t4\_t2}_i \\ \text{diff\_t4\_t3}_i \\ \text{diff\_t4}_i \\ \text{resSD}_i \end{bmatrix}}_{\boldsymbol{\phi}(i)} \sim \text{tform}\left\{ \text{N}\left(\begin{bmatrix} \text{raw\_pracEffect} \\ \text{raw\_mm\_Trial\_1} \\ \text{raw\_mm\_Trial\_2} \\ \text{raw\_mm\_Trial\_3} \\ \text{raw\_mm\_Trial\_4} \\ \text{raw\_selfFeedback\_practice} \\ \text{raw\_selfFeedback} \\ \text{raw\_diff\_t1} \\ \text{raw\_diff\_t2\_t1} \\ \text{raw\_diff\_t2} \\ \text{raw\_diff\_t3\_t1} \\ \text{raw\_diff\_t3\_t2} \\ \text{raw\_diff\_t3} \\ \text{raw\_diff\_t4\_t1} \\ \text{raw\_diff\_t4\_t2} \\ \text{raw\_diff\_t4\_t3} \\ \text{raw\_diff\_t4} \\ \text{raw\_resSD} \end{bmatrix}, \begin{bmatrix}
\text{rawPCov\_1\_1} & \text{rawPCov\_2\_1} & \text{rawPCov\_3\_1} & \text{rawPCov\_4\_1} & \text{rawPCov\_5\_1} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
\text{rawPCov\_2\_1} & \text{rawPCov\_2\_2} & \text{rawPCov\_3\_2} & \text{rawPCov\_4\_2} & \text{rawPCov\_5\_2} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
\text{rawPCov\_3\_1} & \text{rawPCov\_3\_2} & \text{rawPCov\_3\_3} & \text{rawPCov\_4\_3} & \text{rawPCov\_5\_3} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
\text{rawPCov\_4\_1} & \text{rawPCov\_4\_2} & \text{rawPCov\_4\_3} & \text{rawPCov\_4\_4} & \text{rawPCov\_5\_4} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
\text{rawPCov\_5\_1} & \text{rawPCov\_5\_2} & \text{rawPCov\_5\_3} & \text{rawPCov\_5\_4} & \text{rawPCov\_5\_5} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
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0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0
\end{bmatrix} \right) + \underbrace{\begin{bmatrix} \text{raw\_pracEffect\_agez} \\ \text{raw\_mm\_Trial\_1\_agez} \\ \text{raw\_mm\_Trial\_2\_agez} \\ \text{raw\_mm\_Trial\_3\_agez} \\ \text{raw\_mm\_Trial\_4\_agez} \\ \text{raw\_selfFeedback\_practice\_agez} \\ \text{raw\_selfFeedback\_agez} \\ \text{raw\_diff\_t1\_agez} \\ \text{raw\_diff\_t2\_t1\_agez} \\ \text{raw\_diff\_t2\_agez} \\ \text{raw\_diff\_t3\_t1\_agez} \\ \text{raw\_diff\_t3\_t2\_agez} \\ \text{raw\_diff\_t3\_agez} \\ \text{raw\_diff\_t4\_t1\_agez} \\ \text{raw\_diff\_t4\_t2\_agez} \\ \text{raw\_diff\_t4\_t3\_agez} \\ \text{raw\_diff\_t4\_agez} \\ \text{raw\_resSD\_agez} \end{bmatrix}}_{\boldsymbol{\beta}} \underbrace{\begin{bmatrix} \text{agez} \end{bmatrix}}_{\mathbf{z}} \right\}
$$

Initial latent state:

$$
\underbrace{\begin{bmatrix} \text{practice} \\ \text{t1} \\ \text{t2} \\ \text{t3} \\ \text{t4} \end{bmatrix}(t_0)}_{\boldsymbol{\eta}(t_0)} \sim \text{N}\left(\underbrace{\begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}}_{\text{T0MEANS}}, \underbrace{covsdcor\left\{ \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix} \right\}}_{\underbrace{\mathbf{Q}^*_{t0}}_{\text{T0VAR}}} \right)
$$

Deterministic change:

$$
\underbrace{\text{d}\begin{bmatrix} \text{practice} \\ \text{t1} \\ \text{t2} \\ \text{t3} \\ \text{t4} \end{bmatrix}(t)}_{\text{d}\boldsymbol{\eta}(t)} = \left(\underbrace{\begin{bmatrix} \text{selfFeedback\_practice} & 0 & 0 & 0 & 0 \\ 0 & \text{selfFeedback} & 0 & 0 & 0 \\ 0 & 0 & \text{selfFeedback} & 0 & 0 \\ 0 & 0 & 0 & \text{selfFeedback} & 0 \\ 0 & 0 & 0 & 0 & \text{selfFeedback} \end{bmatrix}}_{\underbrace{\mathbf{A}}_{\text{DRIFT}}} \underbrace{\begin{bmatrix} \text{practice} \\ \text{t1} \\ \text{t2} \\ \text{t3} \\ \text{t4} \end{bmatrix}(t)}_{\boldsymbol{\eta}(t)} + \underbrace{\begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}}_{\underbrace{\mathbf{b}}_{\text{CINT}}} + \underbrace{\begin{bmatrix} 1 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}}_{\underbrace{\mathbf{M}}_{\text{TDPREDEFFECT}}} \underbrace{\begin{bmatrix} \text{practice} \end{bmatrix}}_{\boldsymbol{\chi}(t)} \right) \text{d}t \; +
$$

Random change:

$$
\underbrace{cholsdcor\left\{ \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & \text{diff\_t1} & 0 & 0 & 0 \\ 0 & \text{diff\_t2\_t1} & \text{diff\_t2} & 0 & 0 \\ 0 & \text{diff\_t3\_t1} & \text{diff\_t3\_t2} & \text{diff\_t3} & 0 \\ 0 & \text{diff\_t4\_t1} & \text{diff\_t4\_t2} & \text{diff\_t4\_t3} & \text{diff\_t4} \end{bmatrix} \right\}}_{\underbrace{\mathbf{G}}_{\text{DIFFUSION}}} \underbrace{\text{d}\begin{bmatrix} W_1 \\ W_2 \\ W_3 \\ W_4 \\ W_5 \end{bmatrix}(t)}_{\text{d}\mathbf{W}(t)}
$$

Observations:

$$
\underbrace{\begin{bmatrix} \text{Trial\_1} \\ \text{Trial\_2} \\ \text{Trial\_3} \\ \text{Trial\_4} \end{bmatrix}(t)}_{\mathbf{Y}(t)} = \underbrace{\begin{bmatrix} \text{pracEffect} & 1 & 0 & 0 & 0 \\ \text{pracEffect} & 0 & 1 & 0 & 0 \\ \text{pracEffect} & 0 & 0 & 1 & 0 \\ \text{pracEffect} & 0 & 0 & 0 & 1 \end{bmatrix}}_{\underbrace{\boldsymbol{\Lambda}}_{\text{LAMBDA}}} \underbrace{\begin{bmatrix} \text{practice} \\ \text{t1} \\ \text{t2} \\ \text{t3} \\ \text{t4} \end{bmatrix}(t)}_{\boldsymbol{\eta}(t)} + \underbrace{\begin{bmatrix} \text{mm\_Trial\_1} \\ \text{mm\_Trial\_2} \\ \text{mm\_Trial\_3} \\ \text{mm\_Trial\_4} \end{bmatrix}}_{\underbrace{\boldsymbol{\tau}}_{\text{MANIFESTMEANS}}} + \underbrace{\begin{bmatrix} \text{resSD} & 0 & 0 & 0 \\ 0 & \text{resSD} & 0 & 0 \\ 0 & 0 & \text{resSD} & 0 \\ 0 & 0 & 0 & \text{resSD} \end{bmatrix}}_{\underbrace{\boldsymbol{\Theta}}_{\text{MANIFESTVAR}}} \underbrace{\begin{bmatrix} \epsilon_1 \\ \epsilon_2 \\ \epsilon_3 \\ \epsilon_4 \end{bmatrix}(t)}_{\boldsymbol{\epsilon}(t)}
$$

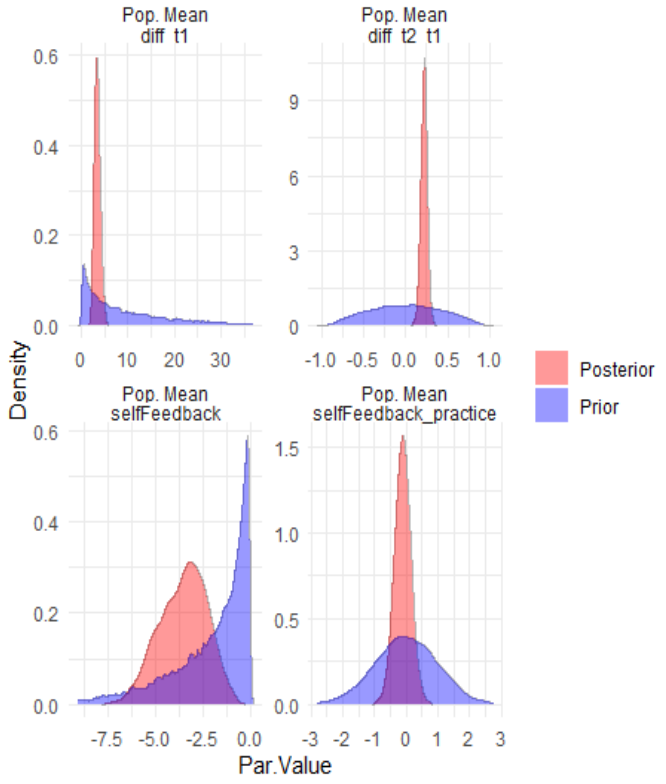
Latent noise per time step: $\Delta\left[W_{j\in[1,5]}\right](t-u) \sim \text{N}(0, t-u)$ Observation noise: $\left[\epsilon_{j\in[1,5]}\right](t) \sim \text{N}(0,1)$

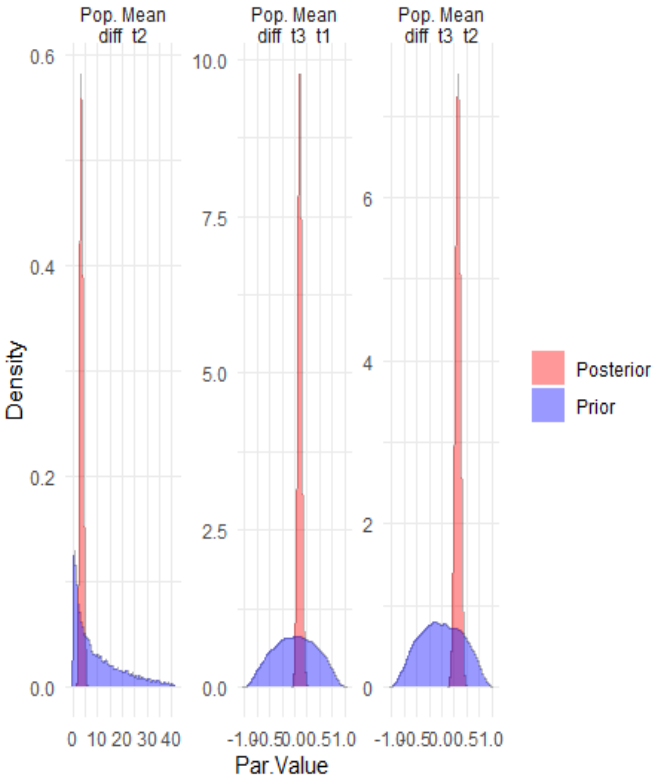
cholsdcor converts lower tri matrix of std dev and unconstrained correlation to Cholesky factor covariance.

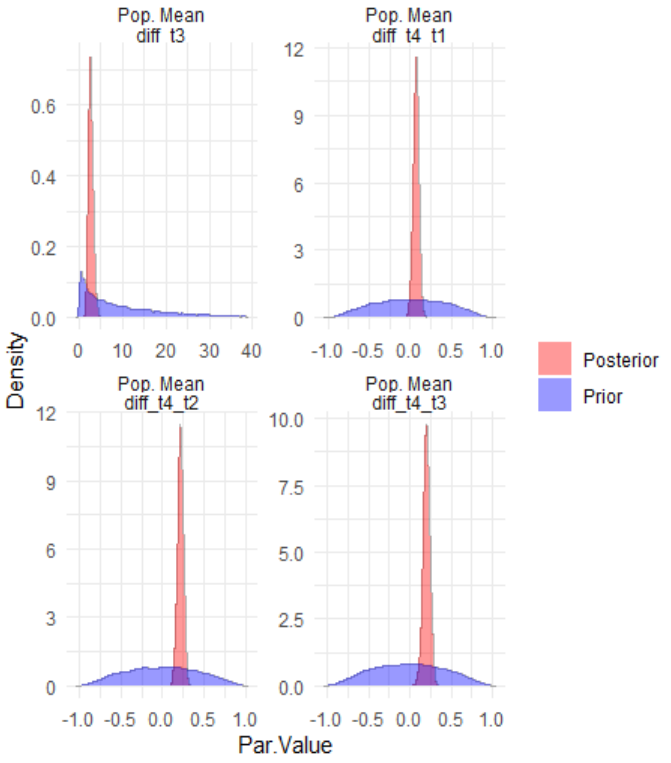
covsdcor = transposed cross product of cholsdcor, to give covariance.

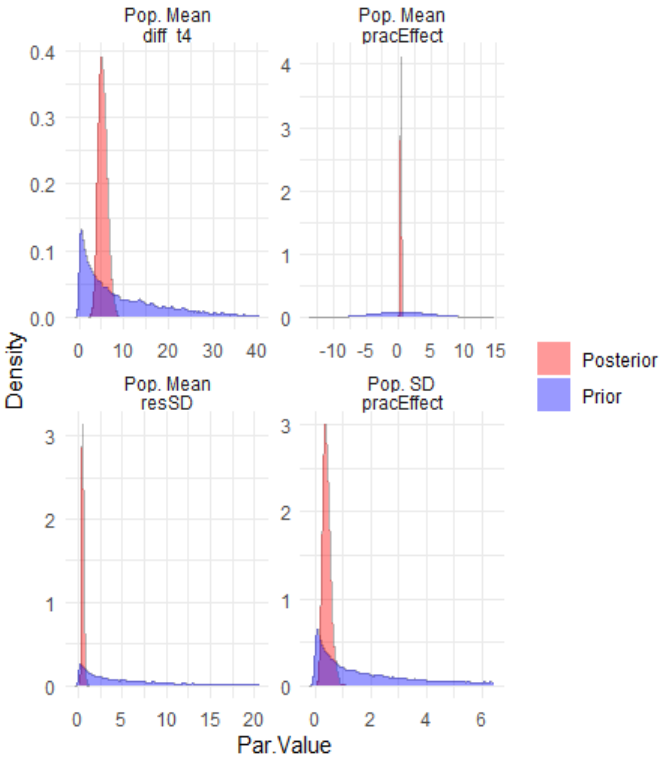
See Driver & Voelkle (2018) p11.

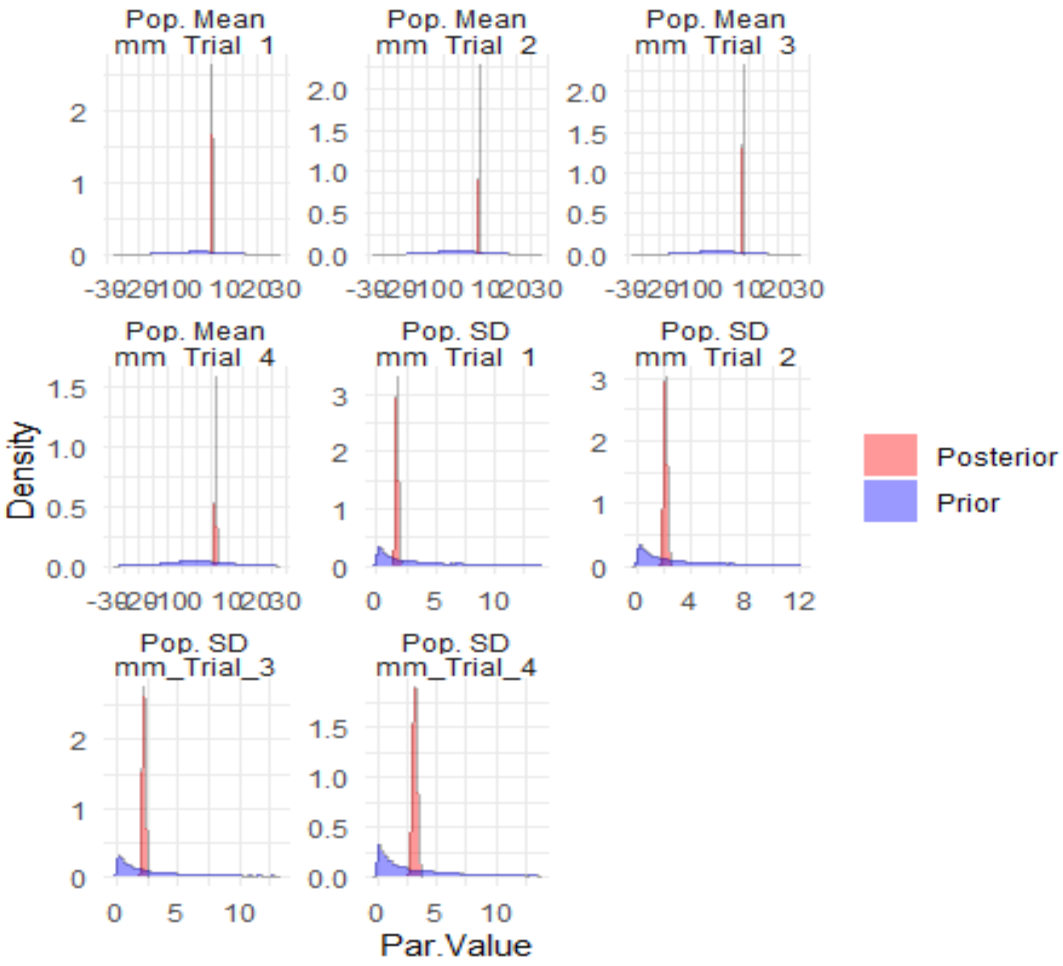
The following plots show prior and posterior distributions of model parameters:










Pop. Mean mm Trial 1
Pop. Mean mm Trial 2
Pop. Mean mm Trial 3
Pop. Mean mm Trial 4
Pop. SD mm Trial 1
Pop. SD mm Trial 2
Pop. SD mm_Trial_3
Pop. SD mm_Trial_4
Density
Par.Value
Posterior
Prior