GENERAL

analysing repeated measures with linear mixed models

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Analysing Repeated Measures with Linear Mixed Models: A Comprehensive Guide

In many research fields—psychology, medicine, ecology, and social science—data are collected repeatedly from the same subjects over time or across related conditions. These **repeated measures** designs capture the dynamic nature of the phenomenon under study but also introduce statistical challenges such as correlated observations and varying numbers of measurements per subject. Traditional methods like repeated measures ANOVA struggle when data are unbalanced, missing, or when the covariance structure is complex. **Linear mixed models (LMMs)** provide a flexible, robust framework that accommodates these intricacies by explicitly modeling both fixed effects (population level predictors) and random effects (subject specific deviations). This article offers a deep dive into the theory, practical implementation, and best practices for analysing repeated measures using linear mixed models.

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What Are Repeated Measures?

Repeated measures arise when the same experimental unit—be it a person, animal, plant, or measurement device—is observed multiple times. These observations are typically taken at different time points, under varying conditions, or across multiple sites. The key characteristic is that each unit contributes a cluster of correlated observations, violating the independence assumption of many conventional statistical models.

Examples of Repeated Measures Designs

- Longitudinal studies tracking patient health over months or years.
- Within subject experiments where each participant experiences all treatment levels.
- Panel data in economics where households are surveyed annually.
- Multi site measurements of environmental variables across several locations over time.

Challenges of Repeated Measures Data

While repeated measures provide rich information, they also pose several statistical challenges:

1. Correlation among observations—measurements within a subject are not independent.
2. Unbalanced data—different subjects may have varying numbers of observations.
3. Missing data—dropouts or intermittent missingness are common.
4. Complex covariance structures—variances may differ across time points, and correlations may decay over time.
5. Time varying covariates—predictors that change over time require careful handling.

Ignoring these issues can inflate Type I error rates, reduce statistical power, and lead to biased estimates.

Introduction to Linear Mixed Models

Linear mixed models extend the familiar linear regression framework by incorporating random effects. They can be written in matrix form as:

y = X;" ² ¦" ² µ

- y is the vector of observed responses.
- X is the design matrix for fixed effects.
- ;" —2 F†R `ector of fixed effect coefficients.
- Z is the design matrix for random effects.
- b is the vector of random effect coefficients, assumed to follow a multivariate normal distribution.
- ;R —2 F†R `ector of residual errors.

By specifying appropriate random effect structures (e.g., random intercepts, random slopes), LMMs capture the within subject correlation and allow for individual variation in baseline levels and trajectories.

Specifying an LMM

Choosing the right model specification is a balance between parsimony and fidelity to the data generating process. The main components to decide upon are:

- Fixed effects—variables of primary scientific interest (e.g., treatment, time).
- Random effects—subject specific deviations that account for correlation.
- Covariance structure—how residuals are correlated across time or conditions.

Fixed Effect Choices

Fixed effects capture the average population trend. Common choices include:

- Time or age (continuous or categorical).
- Treatment group or intervention.
- Interaction terms (e.g., treatment × time).
- Covariates such as baseline characteristics.

Random Effect Choices

Random effects allow each subject to deviate from the overall fixed effect pattern. Typical structures:

- Random intercepts—each subject has its own baseline.
- Random slopes—each subject has its own rate of change over time.
- Combination of intercepts and slopes.

Covariance Structures for Residuals

Residuals may still be correlated after accounting for random effects. Common structures:

- Unstructured (UN)—each pair of time points has its own covariance.
- Compound symmetry (CS)—constant variance and equal covariance across time.
- Autoregressive (AR(1))—covariance decays exponentially with lag.
- Toeplitz, heterogeneous CS, etc.

Choosing the appropriate structure depends on theoretical considerations and model fit criteria.

Random Effects Structures

Random effects capture the hierarchical nature of repeated measures data. The selection of random effect components is guided by:

1. Scientific rationale—does the theory suggest individual variation in baseline or slope?
2. Data structure—does the dataset support estimation of random slopes (e.g., enough time points per subject)?
3. Model comparison—use likelihood ratio tests (LRT) or information criteria (AIC, BIC) to compare nested models.

Random Intercept Model

Assumes each subject has a unique baseline but shares the same slope:

y_{ij} = ;#Ç7V#ã Â÷7V#â ² ²₁X_{ij} + b_{0i} + ;SÇ7V#æ–£Â÷7V#à

where *b_{0i} ~ N(0, <3Ç7V#æ#Â÷7V#ãÇ7W ã#Â÷7W â•*

Random Slope Model

Allows both baseline and slope to vary across subjects:

y_{ij} = ;#Ç7V#ã Â÷7V#à + ;#Ç7V#ã Â÷7V#åƒÇ7V#æ–£Â÷7V#à + b_{0i} + b_{1i}X_{ij} + ;SÇ7V#æ–£Â÷7V#à

with *(b_{0i}, b_{1i}) ~ MVN(0, :3Ç7V#æ#Â÷7V#â•*

Cross Random Effects

In multi level designs, random effects may be nested or crossed (e.g., patients nested within clinics).

Covariance Structures

The residual covariance matrix can be specified to reflect the expected pattern of correlation among repeated measures. Some commonly used structures:

- Unstructured (UN)—most flexible, but requires many parameters.
- Compound Symmetry (CS)—assumes equal correlation across all time points.
- Autoregressive (AR(1))—captures decaying correlation with time lag.
- Toeplitz—different correlations for each lag.
- Heterogeneous CS (HCS)—allows variances to differ across time while keeping constant correlation.

Model fit metrics and theoretical justification should guide the choice.

Model Selection and Estimation

Model selection in the context of LMMs involves balancing fit and complexity. Two main approaches are:

1. Likelihood based comparison—use the likelihood ratio test (LRT) for nested models.
2. Information criteria—AIC, BIC, or DIC (for Bayesian models).

When using REML (restricted maximum likelihood) for estimation, note that AIC and BIC values are only comparable among models with the same fixed effects structure.

Estimation Methods

- Maximum Likelihood (ML)—provides unbiased fixed effect estimates but can over penalize random effect variance.
- REML—preferred for estimating variance components; corrects for fixed effect degrees of freedom.
- Bayesian estimation—uses priors and MCMC; flexible for complex hierarchical models.

In practice, most software implements REML by default for mixed effects models.

Interpreting Results

Understanding the output of an LMM requires attention to both fixed and random components.

Fixed Effects

Fixed effect coefficients represent the average population effect. For example, a coefficient of 0.5 for time indicates that, on average, the outcome increases by 0.5 units per time unit.

Random Effects

The variance components describe the spread of random intercepts and slopes. A large random intercept variance suggests substantial between subject variability in baseline levels.

Intraclass Correlation Coefficient (ICC)

The ICC quantifies the proportion of total variance attributable to between subject differences:

ICC = <3Ç7V#æ#Â÷7V#ãÇ7W ã#Â÷7W â ò ƒÃ_b² + <3Ç7V#ãµ</sub>²)

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