



# Improved confidence intervals for nonlinear mixed-effects and nonparametric regression models

Nan Zheng<sup>1</sup> · Noel Cadigan<sup>2</sup>

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## Abstract

Statistical inference for high-dimensional parameters (HDPs) can leverage their intrinsic correlations, as spatially or temporally close parameters tend to have similar values. This is why nonlinear mixed-effects models (NMMs) are commonly used for HDPs. Conversely, in many practical applications, the random effects (REs) in NMMs are correlated HDPs that should remain constant during repeated sampling for frequentist inference. In both scenarios, the inference should be conditional on REs, instead of marginal inference by integrating out REs. We summarize recent theory of conditional inference for NMM, and then propose a bias-corrected RE predictor and confidence interval (CI). We also extend this methodology to accommodate the case where some REs are not associated with data. Simulation studies indicate our new approach leads to substantial improvement in the conditional coverage rate of RE CIs, including CIs for smooth functions in generalized additive models, compared to the existing method based on marginal inference.

**Keywords** Confidence interval · Nonlinear mixed-effects model · Prediction error · State-space model · Generalized additive model · Template model builder

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✉ Noel Cadigan  
Noel.Cadigan@mi.mun.ca

<sup>1</sup> Department of Mathematics and Statistics, Memorial University of Newfoundland, St. John's, NL A1C 5S7, Canada

<sup>2</sup> Centre for Fisheries Ecosystems Research, Fisheries and Marine Institute of Memorial University of Newfoundland, St. John's, NL A1C 5R3, Canada