Population-Based Sequential Data Assimilation for Oncology Modeling : Theory and Practical Illustrations

Annabelle COLLIN, Laboratoire Jean Leray - Nantes

Accurate parameter estimation in mathematical models is essential for biomedical applications, particularly for describing tumor dynamics by combining mechanistic modeling with available data. Repeated measurements across individuals (patients or biological experiments for example), within a mixed-effects framework [1], can enhance the estimation. In this framework, model parameters are decomposed into fixed effectsrepresenting the typical behavior in the populationand random effects-capturing individual variability. Estimation is then performed by pooling all subject measurements together and estimating a global distribution of uncertainties in the population.
To illustrate this approach, we begin with a simpler case : an ordinary differential equation (ODE) model of tumor growth, applied to a large cohort of patients with meningiomasbenign brain tumors [2]. While such strategies are well established in ODE modeling, extending them to partial differential equations (PDEs) presents significant challenges. In tumor modeling, PDEs are often necessary to capture spatial dynamics, but the combination of high dimensionality, sparse data, and measurement noise makes classical mixed-effects estimation computationally prohibitive in practice.
To address this issue, we propose an estimation strategy specifically designed for PDE models with repeated measurements. This method builds on two key concepts : (1) a population-based Kalman filter [3] and (2) joint state-parameter estimation [4]. In this framework, uncertainties in the model states - such as unknown initial conditions - are managed using a Luenberger observer, while parameter estimation is performed via a reduced-order Kalman filter operating in the parameter space, leveraging repeated data across similar subjects.
The effectiveness of the approach is demonstrated through numerical simulations and experimental data on tumor spheroid electroporation, highlighting its relevance in applications where reconstructing spatial tumor dynamics from sparse or noisy observations is crucial [5].

Références

[1] Comets, Emmanuelle, Audrey Lavenu, and Marc Lavielle. *Parameter estimation in nonlinear mixed effect models using saemix, an R implementation of the SAEM algorithm.* Journal of Statistical Software 80 (2017) : 1-41.

[2] Collin, Annabelle, et al. *Spatial mechanistic modeling for prediction of the growth of asymptomatic meningiomas.* Computer Methods and Programs in Biomedicine 199 (2021) : 105829.

[3] Collin, Annabelle, Mélanie Prague, and Philippe Moireau. *Estimation for dynamical systems using a population-based Kalman filterApplications in computational biology.* MathematicS In Action 11.1 (2022) : 213-242.

[4] Moireau, Philippe, Dominique Chapelle, and Patrick Le Tallec. *Joint state and parameter estimation for distributed mechanical systems.* Computer methods in applied mechanics and engineering 197.6-8 (2008) : 659-677.

[5] Collin, Annabelle. *Population-based estimation for PDE systemApplications in electroporation of tumor spheroids.* ESAIM : Control, Optimisation and Calculus of Variations 30 (2024) : 30.

Contact : `annabelle.collin@univ-nantes.fr`