Fast and Accurate Parameter Sensitivities for the General Rate Model of Chromatography

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The General Rate Model is widely used for numerical simulation of chromatographic separation of biochemical mixtures in aqueous solutions. The model depends on a range of physical and chemical parameters which must be estimated by fitting simulation results to experimental data. For that purpose efficient gradient-based optimization algorithms naturally require highly accurate parameter sensitivities. We have hence extended an existing solver for providing arbitrary precision sensitivities preserving speed and scalability of the original simulator implementation.

The corresponding forward sensitivity systems of the DAE system can be derived by differentiation with respect to the respective model parameters. Together with appropriate initial conditions, the resulting equation states an initial value problem and can be integrated in time with the original system. For sensitivity analysis our simulator uses a staggered corrector approach, which utilizes previously developed code infrastructure such as the BDF method, analytically treated Jacobian information, and a customized linear solver module. With this approach, parameter sensitivities can be computed arbitrarily accurate provided that the sensitivity residual is evaluated exactly. Our implementation ensures this by using hybrid analytic and algorithmic derivatives.

The user has complete control over sensitivity quality by specifying the wanted integration tolerances. Finite differences are commonly applied for computing the same sensitivities, but require a good guess for the perturbation, which can easily lead to uncontrollable approximation errors. Though the theoretical computational cost of the staggered corrector method is equivalent to finite differences, our implementation performs much better than finite differences, particularly in demanding problems.