
Yasunori Aoki
**Cluster Newton method for Inverse Problems: applied to
Model Parameter Estimation**

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We describe a new method for inverse problem that proceeds by simultaneously finding multiple solutions of the parameter estimation problem. Estimation of the parameter of a finitely parameterized ODE based mathematical model from an experimental data is required in many fields of science. This problem can be thought as solving a system of nonlinear equations

$$\mathbf{f}(\boldsymbol{\theta}) = \mathbf{y}^*, \quad (1)$$

where \mathbf{f} is a map from \mathbb{R}^m to \mathbb{R}^n , $\boldsymbol{\theta}$ is the parameter vector, and \mathbf{y}^* is the experimental data. A standard approach for solving this type of system of nonlinear equations is a gradient based method such as the Newton method or the Levenberg-Marquard method. However, in the case of finding parameters from experimental data the problem may be more complicated than just solving (1) in the following ways, and standard nonlinear solvers may not be adequate:

- There is no guarantee that a solution to (1) exists, nor that it is unique.
- We often do not have a good initial guess for the parameter value $\boldsymbol{\theta}$.
- The experimental data contains a lot of error.

In order to overcome these challenges we have constructed a numerical algorithm called the Cluster Newton method that approximately solves the system of nonlinear equations. This method differs from traditional nonlinear equation solvers in the following ways:

- It find multiple possible solutions that approximately satisfy (1).
- It is more robust against the local minima of the objective function compare to other gradient based algorithms since it constructs a linear approximation from multiple points.

- It is faster than population based stochastic method as it is a gradient base algorithm.

Simply put, the Cluster Newton method combines the desirable properties of a population based global optimization method (like semi-global convergence) and with properties of gradient based method (like convergence speed), as it moves cluster of tentative solution points using gradient like information. We demonstrate these points through two examples of the mathematical models in systems biology, parameter identification of a pharmacokinetics model and influenza kinetics model.

The first example is joint work with Ken Hayami of the National Institute of Informatics and Akihiko Konagaya of the Tokyo Institute of Technology. The second example is joint work with Ben Holder of the Ryerson University.