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Improvements to the Cluster Newton Method for Underdetermined Inverse Problems - Parameter Identification for Pharmacokinetics-

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The Cluster Newton method (CN method) has proved to be very efficient at finding multiple solutions to underdetermined inverse problems. In the case of pharmacokinetics, underdetermined inverse problems are often given extra constraints to restrain the variety of solutions. In this paper, we propose an algorithm based on the two parameters of the Beta distribution to find families of solution near a solution of interest. This allows for a much greater control of the variety of solutions that can be obtained with the CN method. In addition, this algorithm facilitates the task of obtaining pharmacologically feasible parameters. Moreover, we also make some improvements to the original CN method including an adaptive margin of error for the perturbation of the target values and the use of an analytical Jacobian in the resolution of the forward problem.

[1] Aoki, Y., Hayami, K., De Sterck, H., and Konagaya, A., Cluster Newton method for sampling multiple solutions of an underdetermined inverse problem: Parameter identification for pharmacokinetics, *SIAM Journal on Scientific Computing* (accepted for publication) (Preliminary version available as *NII Technical Report*, NII-2011-002E, National Institute of Informatics, Tokyo, 2011, at http://www.nii.ac.jp/TechReports//11-002E.html.)

[2] Gaudreau, P., Hayami, K., Aoki, Y., Safoui, H., and Konagaya, A., Improvements to the cluster Newton method for an underdetermined inverse problem,(submitted, also to appear as a *NII Technical Report*).