FluxEs: An 'R' Framework for Parameter Estimation in Biological Networks

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Abstract

Parameter estimation in biological networks is a difficult task and many computer programs were developed for this purpose. However, available computer methods suffer from lack of easy implementation of new biological pathways. Hence, we have designed a new framework called *FluxEs* using an object-oriented programming approach, implemented using S4 classes in R. It particularly addresses distribution of isotopes between metabolites in a carbon-transition network useful for quantifying metabolic fluxes. The developed package provides a simple way to specify the topological information of the network as well as the precise transitions of carbon atoms between molecules in plain text files, and guides the user through the optimization process. For the purpose of parameter estimation, *FluxEs* automatically derives the mathematical representation of the formulated network, and assembles a set of ordinary differential equations (ODEs). Afterwards, it fits experimentally measured Nuclear Magnetic Resonance (NMR) multiplet intensities with the metabolic model result, by continuously solving the ODEs numerically, scanning parameter space to obtain optimal parameter estimates. A test was performed by applying *FluxEs* to fit a model of the tricarboxylic acid (TCA) cycle to simulated ^{13}C NMR data, including realistic measurement noise. Flux values could be re-estimated with significant precision. Subsequent flux estimation on experimental NMR data of animal heart biopsies showed good correspondence with independent chemical measurements.