Homogeneity tests for Michaelis-Menten curves with application to fluorescence resonance energy transfer data

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(Submitted on 4 May 2011)

Resonance energy transfer methods are in wide use for evaluating protein-protein interactions and protein conformational changes in living cells. Fluorescence resonance energy transfer (FRET) measures energy transfer as a function of the acceptor:donor ratio, generating FRET saturation curves. Modeling these curves by Michaelis-Menten kinetics allows characterization by two parameters, which serve to evaluate apparent affinity between two proteins and to compare this affinity in different experimental conditions. To reduce the effect of sampling variability, several statistical samples of the saturation curve are generated in the same biological conditions. Here we study three procedures to determine whether statistical samples in a collection are homogeneous, in the sense that they are extracted from the same regression model. From the hypothesis testing viewpoint, we considered an F test and a procedure based on bootstrap resampling. The third method analyzed the problem from the model selection viewpoint, and used the Akaike information criterion (AIC). Although we only considered the Michaelis-Menten model, all statistical procedures would be applicable to any other nonlinear regression model. We compared the performance of the homogeneity testing methods in a Monte Carlo study and through analysis in living cells of FRET saturation curves for dimeric complexes of CXCR4, a seven-transmembrane receptor of the G protein-coupled receptor family. We show that the F test, the bootstrap procedure and the model selection method lead in general to similar conclusions, although AIC gave the best results when sample sizes were small, whereas the F test and the bootstrap method were more appropriate for large samples. In practice, all three methods are easy to use simultaneously and show consistency, facilitating conclusions on sample homogeneity.

Comments:	26 pages, 2 figures
Subjects:	**Biomolecules (q-bio.BM)**; Quantitative Methods (q-bio.QM); Applications (stat.AP)
MSC classes:	62P10, 62J02
Cite as:	arXiv:1105.0780 **[q-bio.BM]**

(or **arXiv:1105.0780v1** **[q-bio.BM]** for this version)

Submission history

From: Amparo Baillo [view email]
[v1] Wed, 4 May 2011 09:59:08 GMT (313kb)

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