

Comparing models and biological data using nonlinear fitting

Omer Dushek

Sir William Dunn School of Pathology, University of Oxford
Centre for Mathematical Biology, University of Oxford

Course Aim. Experimental biologists often need to compare the outcome of multiple treatments when data is collected over multiple doses or time points. Consider the experimental data shown in Fig 1. How do we determine if the two dose-response curves in Fig. 1A or the two time-course curves in Fig. 1B are statistically different? A common approach is to repeat the measurement multiple times at a single dose or time point and perform a relevant statistical test (e.g. a t-test). A drawback of this procedure is that it masks effects that may only be apparent at different doses or time points. These effects, that are dose or time-dependent, often provide useful mechanistic insights. In this tutorial, we explain how to statistically compare multiple treatment curves directly, without the need for repeated measurements, and highlight the utility of the procedure in revealing mechanistic insights. No prior knowledge of mathematical modeling or statistics will be assumed and discussion will be restricted to tools available in Graphpad Prism[®]. Participants are encouraged to bring their own data, which they can analyze with assistance in the last section of the course.

Course Content. The course contains four sections.

1. How to fit biological data to mathematical models (including how to assess the quality of a fit, the effects of noise, and the effects of incomplete data).
2. How to compare multiple models using a single data set.
3. How to compare multiple data using a single model.
4. Case studies and analysis of your own data.

Course Format. Each of the three sections (above) will begin with a lecture followed by a live demonstration in Prism (15 minutes). Participants will then use Prism to carry out exercises themselves (15 minutes). In the last section, participants will analyze three case studies and/or their own data (30 minutes). Instructors will be available throughout the workshop for assistance.

Course Length. The total course length is 2 hours (3 sections that include a 15 minute lecture & 15 minute practical plus 30 minutes of case study analysis).

Participant Numbers. Maximum 35.

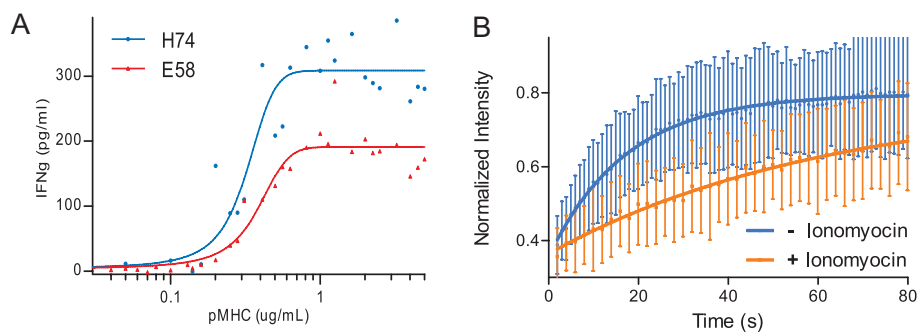


Figure 1: Examples of dose-dependent or time-dependent data to be compared. A) Dose-response data for T cell activation. T cells were incubated with two different ligands at indicated doses for 4 hours, and the concentration of IFN- γ (a secreted cytokine) in the supernatant was measured. B) Fluorescence recovery after photobleaching (FRAP) data for the T cell receptor (TCR), a mobile receptor on the T cell surface. The normalized fluorescence intensity is measured as a function of time for resting T cells or T cells treated with ionomycin, a drug that activates T cells. How do we calculate relevant p-value(s) for statistically comparing the two curves in panels A,B?