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Sim-XL: A Microsoft Excel-Based Organ Bath Simulator

Background and Purpose: Increasing pressures on costs, staff time and laboratory infrastructure mean that today's pharmacology students have limited opportunities to undertake traditional organ bath experiments. In the Manchester B.Sc. Pharmacology programme, for example, students perform experiments on the classic guinea pig ileum preparation in two 3 h practical sessions: a simple concentration-response study in year 1, and a more complex experiment involving Schild analysis in year 2. Despite the robustness of this preparation, the students' lack of familiarity with the preparation sometimes leads to poor results and thus demotivation. In addition, poor data can make it difficult to fully exploit opportunities for active learning of the underlying principles of drug action. To ameliorate these problems, we have for many years supplemented our students' practical work with commercially available organ bath simulation software. However, licensing issues means that students cannot install this software on their own computers. Further, commercial packages offer very little opportunity for user customisation.

Experimental Approach: We have developed a Microsoft Excel based simulation package, Sim-XL, that can be freely distributed to student users and that can be tailored to users' needs without programming knowledge.

Key Results: The base version of Sim-XL is an Excel Workbook simulating the guinea pig ileum preparation. It allows students to perform concentration-response experiments using a range of muscarinic agonists, as well as competitive antagonist experiments using atropine and three "unknown" drugs. Student users are presented with a spreadsheet with drop down menus that allow selection of the drugs to be applied and text boxes for entry of drug concentration. The experimental system is illustrated diagrammatically below the input areas. When a stimulus has been selected, the simulated response is displayed by plotting an Excel graph function over the area occupied by the image of the computer screen. Students can then measure the magnitude of the response by moving their cursor over the plot. Response size is calculated using a simple functional Hill equation with the addition of a decay phase as agonist concentration is increased. Parameters such as the EC_{50} and E_{max} values for drugs are stored in a hidden and locked area of the spreadsheet and are not accessible to student users. A further spreadsheet is provided that illustrates the principles of least-squares non-linear regression. Students input their experimental data and an estimate of the EC_{50} and E_{max} values. The theoretical line corresponding to these values is plotted and the sum of the squared residuals is calculated. The students can then iteratively vary the curve fit parameters to refine the fit and minimise the sum of squares. We find this particularly useful for illustrating curve fitting methods used in packages such as GraphPad Prism.

Conclusions and Implications: Teaching staff can readily tailor the package to their needs by adding additional drugs and by altering the formula used to calculate responses, experiments with positive or negative allosteric modulators can be added. By replacing the organ bath graphics with illustrations of other systems,Sim-XL can also be user-customised to simulate other experimental set-ups, for example two-electrode voltage clamp or patch clamp. Such modifications would allow experiments to be simulated in which the subunit composition of a channel or receptor is varied. The flexibility of Sim-XL should therefore make it useful in a wide range of undergraduate teaching contexts. We are happy to provide free copies of Sim-XL upon request.