INTRODUCTION

Modelling is a commonly used word in sciences and engineering, yet it remains one of the least understood concepts. Mathematical models aid demonstrating relationships between variables. They are used to make predictions and forecasts in time and space (Hsia, 2011; Benzekry et al. 2014; Baggaley et al. 2005). Here, we do not dwell on the specifics of individual example models, but discuss essential guides for mathematical and/or statistical modelling. First, we revisit the basics, the fundamentals and need for modelling. Where do mathematical models come from? Why are scientists fascinated with modelling and how does modelling benefit the world? Fundamentally, mathematical models are used to describe our beliefs about how the world functions. In modelling, these beliefs are translated into mathematical formulations and algorithms. Mathematics is a concise language that requires a set of well-defined rules for manipulations. These rules have been proven for decades and shown to hold true under certain situations. Introduction of computers has made calculations simpler and much faster.

We need modelling to understand the nature of, and make predictions on a system's behaviour, motivated by real life applications e.g. in biotechnology (Alon, 2007; Owen and Froman, 1998), agriculture, bio-medical studies etc. Here, we consider a system as an object or a group of objects whose properties are of interest. Although models can never fully replace experiments, they help us answer the specific questions for which they are designed. One should be careful if the model is used to predict an outcome that is beyond the scope of the model. Box and Draper (Box and Draper, 1987) noted that "essentially all models are wrong, but some are useful". Hence, the need to scrutinize for the best performing model to test and validate a hypothesis.

Rule 1: Motivation for modelling

Most real life systems are very complex due to the large number of components in the systems and/or the intricate interactions among them. This leads to system behaviour that is difficult to understand. Mathematical modelling provides a way to understand how quantities vary and relate to each other. Finding solutions to real life problems is often the key motivation to applied research using mathematical modelling. To model such a system, you need to gather sufficient knowledge on essential features of the system of interest. Stick to the objectives of the research since they are fundamental to the initial choice of modelling framework. By reading previous related work to the research item, you can obtain useful clues as to what approach is most suitable for dealing with your problem.

We observed a tremendous increase in the number of articles published with the key word “modelling” and/or “modeling” in the titles and abstract (Fig. 1, ~1960-March 2015). Prior to 1960’s very little attention was given to modelling in life sciences and engineering. However, unlike decades ago, today's inter disciplinary research requires scientists to familiarize themselves with the fundamentals of mathematical and statistical modelling.

Rule 2: Clearly state the hypothesis

It is good practice to first list the variables considerably of interest – preferably before the data analysis/modelling. Such a list guides you to identifying any association between variables. Clearly state any hypothesis to be tested, for it is essential for interpreting results from a model output. For instance, statistical approaches like the ANalysis Of VAriance (ANOVA (Owen and Froman, 1998)) and equivalent methods can be used to test for variations of specific
quantities between and within groups. Setting up a good modelling framework requires hypotheses and often modelling involves iteration before obtaining optimal solutions.

Rule 3: Be open-minded
Mathematical modelling requires open-minded thinking and flexibility in approach in order to tackle challenges. Do not take the obvious for granted — many times students do not probe their results rigorously enough. If you have an idea of what to expect as an output from the modelling and you end up with something far out of expectation, then you should not doubt the results, but focus on determining why the result is the way it appears. The emergence of Computational Systems Biology (Kitano, 2002; Breitling, 2012) and Bioinformatics (Luscombe, 2001) have, for instance, demonstrated that collaborative research between experimentalists in the biological and physical sciences and mathematicians/statisticians can address many challenges in life; challenges that are aimed at improving the quality of life of the general population. Be curious and eager to learn new things outside your comfort zone. Do not be reluctant to venture into testing complex but powerful approaches of analysing data, or learning new software — it pays off in the long run.

Rule 4: Less is more — keep it simple
Keep the modelling framework as simple as can be, unless, absolutely necessary — complexity should be avoided. The more complex a model becomes, the more difficult it is to interpret the outputs or parameters in relation to the real life application. It is easier to relate results from simple modelling frameworks to real life science problems. However, sometimes a simple model is not robust enough to capture variations or explain observed outputs in a given measurement; conceivably, some balance between model complexity and simplicity has to be found. Numerous models and tools can be used to address the same problem in modelling. You need to find the appropriate one. In essence, start with simpler models; then sequentially proceed to more complex ones until the model satisfactorily explains observations in your data and/or meets realistic expected outcomes.

Rule 5: Mechanistic or empirical, stochastic or deterministic
It is important to identify whether the modelling approach is mechanistic or empirical; stochastic or deterministic, in modelling bio-systems (Szallasi, 2010). This helps in narrowing down the number of possible models to choose from to address a specific range of problems you are working on. Essentially, modelling not only refers to analytic model assessments (like theoretical mathematicians do), but also in the context of empirical and/or numerical computing. Mechanistic models are very common in theoretical and molecular biology for modelling e.g. cell population (Mudgal, 2006), gene regulation (van Mourik, 2010). Likewise, deterministic and stochastic models are widely applied in, but not limited to, modelling infectious disease dynamics (Baggerly, 2005; Scherer and McLean, 2002). The areas in which these model formalisms can be used are only limited by our imaginations.

Rule 6: Experimental design
Like in statistical experiments, it is good practice to get the experimental design right before moving onto the actual experimentation and data acquisition. This not only saves time and money but goes a long way to ensure that the modelling results can be relied upon. Models often have parameters that may have to be estimated from data. Only well-designed experiments may provide sufficient reliable information to explain the behaviour of a system. Compare model results with experimental data for any anomalies. If they disagree, then one should renew the hypotheses and improve the model.

Models guide experiments, not the contrary; hence, it is essential to pay attention to good experiment design prior to data collection. According to Fisher (Fisher, 1938):

“To call in the statistician after the experiment is done may be no more than asking him to perform a post-mortem examination: he may be able to say what the experiment died of.”

This hints to how good results can be obtained by methodologically paying attention to details and being thorough in how: experiments are done, data collection, analysis and interpretation.

Rule 7: Be thorough, objective but realistic
To ensure that the research questions and hypothesis of interest are actually assessed as intended, a double check as to whether the model outputs, predictions, estimated parameters actually make sense is recommended. This check is essential for fine-tuning models if large deviations exist in the expected outputs or explaining peculiar results. A clear statement of the assumptions used for each model should be made; this enables a more evaluation of the model performance to assess its weakness, strength and overall robustness based on specific working assumptions under consideration. Realistically, modelling requires knowledge of several subjects, namely: biology, mathematics, computer simulation, etc. For those who are unfamiliar with modelling, a thorough look at literature and/or regular consultative discussions with experts in modelling is strongly recommended.

Not all modelling involves the use of measured data. In some fields of science and engineering it is challenging to collect data; hence; they heavily rely on modelling and simulations. For instance: nanotechnology and quantum physics deals with quantities of minute scales; astrophysics — with objects of extremely large sizes; in vivo measurements in biomedical sciences; design and testing of robots in space and planetary sciences. These disciplines require extremely powerful mathematical models and super-computers for rigorous analysis and predictions. Hence, in modelling, be realistic and aware of the scale of the problem and limitations of the available models. This provides insight on how to deal with associations between physical quantities and devise realistic assumptions for the modelling.

Rule 8: Implementation of models
A good modelling framework can be obtained by not only paying attention to details, but also ensuring that the primarily essential modelling approaches and platform are identified before the model implementation. Properly mapping out a skeletal route-map of how to implement the model, and identification of which software to use and why is critical. Think of the end-product, is the model output / result displayed in a good format; how do the graphs, tables look; are they easily interpretable to the end-user. If not, then find an alternative way to display your results. However powerful a model is, if the result is not displayed in an understandable format to the users, then it is of little use.

Rule 9: Model conceptualization
To facilitate efficiency and as a measure of good practice; map out the modelling stages, namely: building, studying, testing and using phases, it ensures that errors in the model building can be easily traced back and computer codes can be debugged accordingly. Meticulous planning and always keeping the end product in mind is essential, since it acts as a directive as to what the
final results/model outputs should be.

**Rule 10: Choice of software – analysis platform**

Choose whether to use open-source software or not, many tools have built in tool-boxes and libraries. Upon identification of the libraries of interest, you only have learn how it works and what parameters are required; hence, no need to program to implement the model, this way you avoid re-inventing the wheel. Modellers are familiar with most available software, and can easily guide you to a specific assortment of models/libraries to use. Software like R, Python, C, C++, Perl, Java, Matlab, Genstat, SAS, SPSS, COMSOL, MAPLE etc. can be used to analyse various large and complex data. Analysis of such data would be painfully slow and time-consuming without the availability of computers. Thankfully, computers have revolutionized the way scientific research has progressed in the last few decades.

Sophisticated mathematical models coupled with intensive simulations has offered a faster and reliable way to get results that would in the past would have been un-imagineable. Here, simulation refers to the application of a model with the intention to devise ways of problem solving for a given system. The use of computing tools is not restricted to mathematicians or those from closely related computations fields of science; most people can learn to use computing software, since most of them are designed with the end-user in mind.

**CONCLUSION**

Mathematical modelling is a fundamental and quantitative way to analyse and comprehend complex real life systems. Notably, modelling is widely used in sciences like chemistry, physics, mathematics and biology. Modelling and simulation is necessary when experiments are complex, involve large data, are expensive and time-consuming. In many sciences and engineering disciplines, strong emphasis is put on combining systems and control theory with mathematical modelling and analysis. Modelling enables prediction of system dynamics, accurate quantification of numbers of for instance biochemical molecules, populations of pathogens (for instance, viruses and bacteria; modelling viral and immune system dynamics (Perelson, 2002); virus-bacterial interactions (Poggiale et al. 2009)) etc. Other areas in which modelling is widely used is process engineering and manufacturing, environmental research and weather prediction; biomedical and drug design studies etc.; the one size fits all approach does not work for modelling (Atkinson et al. 2013). Essentially, caution has to be taken while choosing models; good models are generally simple yet sufficiently robust.

The textual summary in Fig. 2 is representative of commonly used words in scientific articles on modelling in life sciences, physical sciences and engineering.

**References**

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