Abstraction within experimental physiology

Host: We often take scientific research to be absolute truth; however, there are various levels of abstraction that occur. I am choosing to discuss the abstraction that occurs within experimental physiology. This is because it is the field that I have become most interested in over the last few years. One of the first levels of abstraction that occurs is when we are choosing a model to conduct an experiment within. We know the model doesn't perfectly represent the actual phenomenon of interest but how close does it take us? I am joined now by an individual with some experience in model selection. Could you please explain to us how important model selection really is?

Guest #1: Model selection is very important in science in general but specifically it becomes very important in human physiology and the reason for this is because different models often give drastically different results from each other. In other words, results from one model aren't always applicable to real, living humans. For example, if we take one of the simplest models you can use which is cell culture, where you remove cells from a tissue and you grow them inside of some sort of growth medium inside of a petri dish. Then you can apply specific chemical stressors, you can apply UV light, you can apply a bunch of different stressors and see how the cells are going to react. But because the model is so simple, a lot of the reactions that occur, in response to these very simple stressors, aren't applicable to living, breathing humans. And part of this is to do with the homeostatic mechanisms that are involved in human physiology. When you have cell culture sitting in a dish, you don't have the nervous system innervating the tissue, you don't have endocrine hormones being delivered by the blood stream, you don't have paracrine interactions between tissues that lay adjacent to other tissues. So, when you just have one isolated tissue type, some of these homeostatic mechanisms are removed. The results that you get out of these cell culture models are often drastically exaggerated if you would compare that to what would actually occur in a living, breathing animal. So, for that reason, we must be very careful in selecting the proper model for the type of question we want to answer.

Host: I know you said it was just one example but you seem to be bashing the cell culture method quite a bit. Is there a place for such a method?

Guest #1: These cell culture methods can be very effective in answering certain types of questions but they not effective for answering all of the questions we have in physiology. For that reason, we have different models and sometimes researcher get in wrong. They don't choose the most applicable model for the question they have set out to answer.

Host: Thank you for your insights. Let us move now to the next level of abstraction: data analysis. The first steps of data analysis include checking your data for outliers and for anomalies. Here with me now is someone who recently analyzed a data set that contained both of these things. Could you fill us in on this level of abstraction?

Guest #2: So, I think with outliers, it's important to establish what an outlier is prior to starting your study. So, setting up guidelines to determine what is and isn't an outlier so when one comes up you can immediately determine that it is an outlier and so it doesn't skew with your data during analysis. It's also important to differentiate between an anomaly and an outlier.

Anomalies can come from improper instrumentation, even just problems with the instrumentation itself, whether it's an old machine or the software isn't quite calibrated. So. Its important to be able to distinguish if a data point is an anomaly or an outlier. And then how you would approach those definitely differs depending on your study. In one particular study, we had a participant come in and they didn't meet any of our exclusion criteria. So, we didn't anticipate that the data would be skewed in any way but upon analysis we realized that there was a factor that we hadn't accounted for, when recruiting. That significantly altered their results and it was significantly lower than the average trial that we had. So, at that point we had to determine whether or not it was an anomaly or an outlier and we determined, based on the participant history and the factors involved, we deemed it an outlier. So, that's why it's important to sort of have that criteria gong into a study, so you can avoid those sort of subjective decision during analysis.

Host: How often does this kind of bias come into research and how can we, as readers, tell?

Guest #2: The interesting thing with scientific literature is, you never know if you're getting the full story or not. You read a whole paper and everything makes sense and a lot of the times it's very eloquent in the way it's written but the reality of research is, is there's a lot of things that happen that might go against what you think would happen; it might negate your hypothesis. Researchers can manipulate their data in ways to support their hypotheses and a reader would never know.

Host: That is a very scary thought, for sure. Thank you for taking us through that. The last step of abstraction that occurs happens at the level of data interpretation and presentation. To discuss these to issues, I have our next guest on the line. Take it away.

Guest #3: One very important step in experimental physiology occurs after the data has been collected, after you've removed outliers, after you've adjusted the data to maybe the baseline values and now it's your time to run statistical tests on your data, it's time to put it into figures and publish it into a manuscript. Abd there's a lot of fishy things that can go on in these last final steps of experimental physiology. The first one that I hinted at was the statistical tests that you use. There are tonnes and tonnes of different statistical tests that can be applied to a given data set. And certain statistical tests are more likely to give a type one error and some are more likely to give a type two error. This is basically saying that some are more likely to give a false positive and show a trend when there isn't one and some are more likely to give a false negative or to not give strength to a tend that is actually present. So, people have to be very careful in their choice of statistical test, if they want to be honest with their data. And it's actually happened before where people will take a data set and they'll run hundreds of different statistical tests until they find one that supports their hypothesis and tells the story that they want to tell. And this is something that happens behind closed doors and is something that's not immediately obvious to those who are, say, reading a manuscript or listening to a research presentation. So, this is a step in experimental physiology that can obscure form the truth and can take away from the purity of the experiment.

Host: You talked a lot about the abstraction that occurs at the level of statistical tests but could you briefly go into the problems that occur while publishing a manuscript?

Guest #3: Another important step is actually compiling a manuscript. So, how you choose to present your data. And one of the things that can occur is all the way down to how someone titles their manuscript. There's often these declarative titles that have a clear message in their title but then when your read further into the manuscript, you realize that the actual claim they were making, in their title, wasn't supported significantly. They may have seen a slight change in something and it's okay to state that but if you read it, it's actually not a significant change, statistically speaking. So, if you were just reading the title of manuscripts or just briefly reading through the abstract of a manuscript, you might be pushed to believe something that's actually not validated by the experiment. So, these are just a couple of things that can occur in actually presenting data and interpreting data and they can introduce researcher bias and they can introduce abstraction from what is actually occurring in the real world.

Host: Thank you for that. These three interviews have helped to uncover some of the abstraction occurs within experimental physiology. If we, as readers, keep these things in mind, we can better understand he implications of individual studies.