Expectations vs. Observations and Inference

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Response to Dr. Marc Tollis

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Introduction

What sort of assumptions, lines of thinking, or "common sense" do you take for granted on a day-by-day basis? What sources of authority does one trust and what sort of affects does this has on the public's perception of the general fields of research and study? For the second lecture of the "Research Methods in Informatics and Computing" course (aka. INF501), Dr. Mark Tollis presented a topic under the field of bioinformatics. I believe his presentation fleshed out aspects of these thoughts well.

For the presentation, Dr. Tollis submitted two research papers to read in preparation. The first of the two papers, "Comparative Genomics Reveals Accelerated Evolution in Conserved Pathways during the Diversification of Anole Lizards", discusses his research on determining the evolutionary rate of the anole lizard [1]. This paper introduces "comparative genomics", comparing DNA reference genomes between organisms to gain more knowledge about the functions of genes. In particular, he uses this technique to infer the DNA mutation rate of the anole lizard.

The latter of the two papers, "Evolution of cancer suppression as revealed by mammalian comparative genomics" (2017) [2, p. 5], reflected on the idea of "Peto's paradox" in relation to mammals. The idea of "Peto's paradox" is that one would presume larger organisms with much cells would suffer from much more cellular division and thus more risk cancerous mutations. (For instance, consider an African Savannah elephant compared to a common brown rat just in cell count alone).

In addition to these papers, Dr. Tollis submitted his presentation slides for reference. Please keep in mind that some material being responded to are, as of this writing, still *in prep* (and so have not been submitted to a journal yet). Both topics will be up for discussion further on. More specifically, this response will relate both the tuatara evolutionary rate and Peto's paradox in the context of expectations vs. observations.

Tuatara Rate Debate

From the presentation, Dr. Tollis introduced the topic of the "Tuatara Rate Debate" that took place between 2008 and 2009. The tuatara is the only member of the order *Rhynchocephalia* [3]. This animal had split off from the sister group of squamates (which includes modern lizards and snakes) roughly 220 million years ago. Its relatively old age from the fossil record has garnered intense interest in both biology and bioinformatics. A study in 2008 had shown that the DNA evolutionary rate appeared to be faster than most, if not all, vertebrates examined at the time.

The public took notice of this discovery, as represented by some articles like that from Ars Technica [4]. However, recently more scrutiny has been placed on this conclusion. Using the same techniques of comparative genetics and the Anolis lizard genome as reference [1], Dr. Tollis found contradictory results. Their tentative conclusion, at the time of this writing, is that the tuatara is in fact the *slowest* evolving Lepidosaur (the subclass including tuatara and separately squamates). What I find interesting is how despite this notion of the tuatara to be such a record holder, it is important to take such conclusions with new advances in research and scientific methodologies.

Peto's Paradox

One of the core themes of the presentation was that of paradoxes, in particular "Peto's Paradox". Several factors for increased cancer rate were given, such as caloric intake, growth factors, and just the pure number of cells that made up the organism [3]. However, as stated by Peto's Paradox, there is no observed trend of higher cancer mortality rates relative to body size on a general and macroevolution perspective. While there are a couple approaches to cancer suppression, more focus was given toward apoptosis as an explanation for this paradox.

The pressures presented were intrinsic vs. extrinsic mortality. It is hypothesized that with larger mammals, for instance, there are inherently less extrinsic forces that could cause death; these factors place natural selective pressure on intrinsic causes of death, such as senescence and tumors. So then, the larger the animal is, the less likely they are to die from an earlier onset of cancer, right?

This is yet another example of having to be careful with expectations vs. observations and inference. As mentioned in the concluding statements of Dr. Tollis' paper on mammalian comparative genomics [2, p. 6], one such contradictory observation is that of birds. Modern genomics describes avian dinosaurs as having branched off non-avian dinosaurs in the Jurassic period [3]. However, despite having drifted off toward a general trend of smaller body sizes, birds suffer from an incidence of cancer that is "lower in birds than mammals (1.9% versus 2.8%, respectively)" [2, p. 6].

Conclusions and Thoughts

How these various conclusions can be made on the same specific topics of science is what caught my attention the most about Dr. Tollis' talk. For instance, what fascinated was how the tuatara's evolutionary rate was considered to statement of fact in the public eyes just 10 years ago; yet, if Dr. Tollis' conclusions are true, then this new "common knowledge" is already disputed. What was even more engaging were the various expectations vs. observed results on just the relationship of animal body size to cancer mortality rate. Now I must consider the assumptions I make in my own research, and what sort of potentially misguided conclusions I could make given the wrong assumptions. Given Dr. Tollis' presentation of his own research, I am forced to confront how I go about mine moving forward.

References

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