Modeling of T Cells in Autoimmune Diabetes: Whitepaper

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Importance

Autoimmune diabetes, or type 1 diabetes, is a chronic disease that causes high blood glucose levels; this type of diabetes is an autoimmune disorder, where the immune system attacks healthy body tissue, leading to symptoms [1]. Furthermore, no screening test exists for this disease, which can only be diagnosed after symptoms appear [1].

Background

In type 1 diabetes, pancreatic beta cells do not produce enough insulin, a hormone used by cells to take glucose from the blood; thus, sugar builds up and cells cannot use glucose for energy, leading to symptoms such as blurry vision and possibly complications such as blindness [1]. The lack of insulin stems from the destruction of the beta cells by the immune system. Research with NOD (non-obese diabetic) mice has demonstrated that the onset of diabetes follows an elevated level of autoreactive T cells in the blood (which destroy beta cells); furthermore, the level of these cells followed a cyclic pattern over time [2]. To better understand this mechanism underlying these oscillations, Mahaffy and Keshet constructed a mathematical model that explained the cause of the phenomenon as a gradual decrease in beta cell level [3].

Mathematical analysis of such models can reveal bifurcations, or qualitative changes in behavior; such findings can be applied to predict similar changes in real-world systems. One type, termed a Hopf bifurcation, is of particular note because when the model parameter is continuously slowly varying, the oscillations this bifurcation normally causes will be delayed and will occur later than expected [4]. Mahaffy's model has a Hopf bifurcation, which is responsible for the oscillating T cell levels, but the researchers did not analyze it with a continuously varying parameter.

What's Not Known

The creators of the model explicitly state the beta cell level slowly varies [3], but did not analyze it by continuously varying the parameter; instead, they looked at the behavior with multiple static values of the level of beta cells. Since having a continuous parameter can change the qualitative behavior of a system, and thus affect the conclusions regarding the validity of a model, conducting this analysis matters – especially as it affects the Hopf bifurcation, which explains the oscillations that experimentally preceded the onset of diabetes [4][3].

Question

As the accuracy of the model would impact the conclusions drawn and possible applications, then naturally this question follows: how does treating the level of beta cells as a *continuously* varying slow parameter affect the qualitative behavior of the immune model, and how can those findings be applied to understanding and predicting autoimmune (type 1) diabetes?

Required Resources

Due to the nature of the model, simulation is certainly doable on commodity computer hardware. Thus, no special equipment is necessary to investigate this question. However, being able to consult with a qualified scientist would help in verifying calculations, interpreting the results, and making better conclusions.

Impact

Analyzing the model with a continuously varying slow parameter could imply new physical behavior to search for; in particular, the ability to delay the onset of oscillations may predict a way to prevent the development of diabetes. Meanwhile, a more accurate model could improve the usefulness of this research in predicting diabetes. On the other hand, if the new model no longer matches the experimental evidence, that would indicate that it may not correctly model the actual behavior of the immune system, thus indicating to researchers that they should focus their efforts elsewhere.

References

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