Uncovering the effects of the immune system and treatments on metabolicpathologies in the malaria infected host

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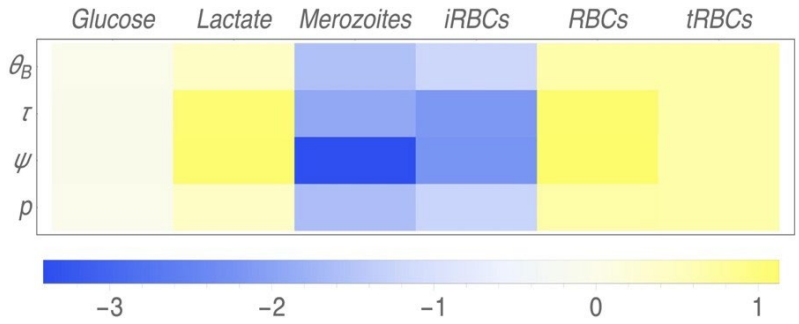

Figure 1*: Sensitivity analysis results for different treatments in a multi-scale malaria model. Four treatments were added to an integrated model that includes the within-host disease dynamics and the metabolism of an infected host. Results indicate the % change in a steady state (top) upon a 1% increase in a treatment strength. The treatments added to the model are: θ_B, an immune enhancement treatment, τ, a transmission blocking treatment, ψ, a treatment that reduces the number of merozoites released per bursting infected red blood cell and, p, an antibody production enhancement treatment.*

Introduction: Malaria presents with clinical symptoms that include fever and anemia, which can partly be attributed to the immune systems response on infection. Clinical features of metabolic markers can additionally indicate life-threatening hypoglycaemia and hyperlactatemia. The aim ofthis project is to analyse the effects of the immune system's response, and that of treatments on the disease and metabolism of a malaria infected host.

Methodology: A within-host disease model [1] has been integrated with a whole-body metabolism model [2] using Wolfram Mathematica. Four different treatments were added to the model and sensitivity analysis was used to investigate the effects of the disease, immune system and treatment parameters on the blood glucose and lactate levels.

Results: Results indicated that the death rates of healthy and infected red blood cells, in addition to the natural synthesis rate of red blood cells, affect the metabolism the most. The blood lactate concentration is substantially more sensitive to disease model alterations than the glucoseconcentration. Results from the sensitivity analysis where treatment is included indicated that all interventions increased the blood lactate levels, which could be correlated to the increase in the total number of red blood cells.

Discussion and Conclusion*:* For this model, an increase in the death rates of healthy and infectedred blood cells could decrease hyperlactatemia but not hypoglycaemia. Furthermore, treatments that act directly on the disease within the host by targeting processes incorporated either into the merozoite or infected red blood cell models have the largest effects on variables within the model, suggesting these as the most viable targeted treatments. The effects of the metabolism on diseaseand the immune system is the next step in the analysis, followed by testing the effects of heterogeneity on the results.

References:

1. Okrinya, A. (2014). 'Mathematical modelling of malaria transmission and pathogenesis',doctoral thesis, Loughborough University, Leicestershire, https://dspace.lboro.ac.uk /2134/17160.
2. Green, K. (2017). 'Whole body modelling of the glucose metabolism in malaria patients', master's thesis, Stellenbosch University, South Africa, http://hdl.handle.net/10019.1/101094.

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