Title

Rbc Lifespan Uncertainty: Models and Anemia Management Robustness

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Abstract

This thesis discusses the modeling of uncertainty of red blood cell (RBC) lifespan distribution in patients suffering from Chronic Kidney Disease(CKD) patients, whose anemia is managed through periodic dosing of erythropoietin (EPO).

In healthy individuals, RBCs containing hemoglobin (Hgb) are produced in the bone marrow. When oxygen carried by hemoglobin is transported to human tissues throughout the body, the kidneys sense reduced level of Hgb and secretes EPO that simulates proliferation of red cell precursors and eventually producing red blood cells. However, in CKD patients, their kidneys fail to secrete enough EPO, so that too few of RBCs are produced to maintain a sufficient Hgb level. As a result, artificial EPO dosing is required when the kidney loses this function to avoid anemia.

To develop effective artificial EPO dosing schemes, it is important to have models of how EPO does dynamically affect hemoglobin levels. Since there is significant uncertainty in this process, it is equally valuable to have mathematical models of such uncertainties, and in this thesis we focus on uncertainty in the lifespan of red blood cells.

In this thesis, we consider two different types of models for RBC lifespan uncertainty: the time-invariant and time-varying cases. In the former, we treat the probabilistic distribution of cell lifespans as fixed for a given patient, but variable (uncertain) over the population. In the latter case, the cell lifespan distribution can change from moment to moment for a given patient.

Amongst several possible choices of RBC lifespan distributions, this thesis will focus on the gamma distribution. For the time-invariant model, a first-order gamma distribution is selected as the nominal distribution, and a multiplicative error model is proposed to analyze the impact of lifespan uncertainty on anemia management.

In the time-varying case, the lifespan distribution is not fixed in time, but allowed to switch over a finite collection of gamma distributions. In other words, each newly-born RBC has a lifespan coming from a distribution chosen from a collection. Both of these models are analyzed so as to evaluate the impact of lifespan uncertainty on the performance of anemia management schemes; including stability and response time.

First Advisor

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