

## BM5063 Mathematical Physiology and Systems Medicine

### Exam 6

#### Instructions

1. This exam is open notes where you can use any hand-written material. Photocopies/prints/books/electronic devices are not permitted to be used.
2. Neatness in the answers is expected.

#### Questions

1. Graves' disease is an autoimmune disease that causes hyperthyroidism in about 1% of the population, usually around middle age. In Graves' disease, the body produces antibodies that activate the TSH receptor, mimicking TSH. As a result, the thyroid produces more thyroid hormones. Modify the HPT axis equations to model Graves' disease. Describe all your assumptions with justifications. What symptoms would you expect in Graves' disease? **(20)**
2. Consider an antigen  $u(t)$  presented by antigen-presenting cells to T cells. This activates effector T cells  $T(t)$  that perform the response functions, and also regulatory T cells denoted  $R(t)$  that inhibit the effector T cells. The dynamics is given by

$$\begin{aligned}\dot{R} &= \alpha_1 u - \beta_1 R \\ \dot{T} &= \alpha_2 \frac{u}{R_0 + R} - \beta_2 T.\end{aligned}$$

- (a) For a given fixed value of  $u$ , draw the phase diagram and identify the fixed points and their stability. **(10)**
- (b) Consider a step-function change in  $u$  from level  $u_1$  to level  $u_2$ . Sketch the change in the levels of  $T$  and  $R$  due to this as a function of time. **(10)**
- (c) Consider another scenario where antigen rises exponentially,  $u(t) = u_0 e^{t/T}$ . What happens to the T cell levels over time? **(10)**