TOPICS IN THE DESIGN OF EXPERIMENTS
PART 1: OPTIMAL DESIGN THEORY
Exercise Sheet 1

Please try to attempt all of the questions. You are welcome to discuss your solutions with me during my office hours.

1. In the example on growth rate, the data were well fitted by a quadratic function $\eta(x;\theta) = \theta_1 + \theta_2 x + \theta_3 x^2$ for $x \in [10, 35]$.
(a) The D-optimum design for the quadratic model defined on $[10, 35]$ is

$$\xi^* = \left\{ \begin{array}{ccc} 10 & 22.5 & 35 \\ \frac{1}{3} & \frac{1}{3} & \frac{1}{3} \end{array} \right\}.$$

Check using the Equivalence Theorem that the design ξ^* is indeed D-optimum and calculate the D-efficiency of the applied design.
(b) Obtain the forms of the c$_{AUC}$-optimality and the c$_{x_{max}}$-optimality criteria for a quadratic model on $[10, 35]$. Comment on the dependence of these criteria on the model parameters.
(c) Calculate numerically the two c-optimum designs. (Hint: Use the Equivalence Theorem for c-optimality and take the least squares estimates of the parameters as the point priors.)

2. Consider the Michaelis-Menten model

$$\eta([S]; V_{max}, K_m) = \frac{V_{max}[S]}{K_m + [S]}.$$

(a) Write down the parameter sensitivities f_1 and f_2.
(b) Show that the D-optimum design points for the model when the maximum concentration is $[S]_{max}$ are

$$[S]_1 = \frac{K_m^o [S]_{max}}{2K_m^o + [S]_{max}} \quad \text{and} \quad [S]_2 = [S]_{max}$$

if the point priors are V_{max}^o and K_m^o.
(c) Find the vertices $(f_1([S]_1), f_2([S]_1))$ and $(f_1([S]_2), f_2([S]_2))$ on the design locus. Evaluate these when $[S]_{max} = 10$, $V_{max}^o = 1$ and $K_m^o = 1$.

3. Suppose that the one-compartment pharmacokinetic model is used with the function

$$\eta(t; k_a, k_e) = \frac{k_a}{k_a - k_e}\left(e^{-k_e t} - e^{-k_a t}\right).$$

(a) Write down the parameter sensitivites at $k_a^o = 0.7$ and $k_e^o = 0.2$.
(b) Show that the D-optimum design points for the model are $t_1 = 1.23$ and $t_2 = 6.86$ for the above point prior.
(c) Calculate the variance function $d(t, \xi^*)$ and verify that $d(t, \xi^*) = 2$ at the support points of the D-optimum design ξ^*.

4. In the general decay model, the differential equation for the concentration of chemical A as a function of time t is

$$\frac{d[A]}{dt} = -k[A]^{\lambda},$$

where k and λ are the rate and order of the reaction.
(a) Show that the solution to the equation is

$$[A] = \{1 - (1-\lambda)kt\}^{1/(1-\lambda)}$$

for $\lambda, k, t \geq 0$ and $\lambda \neq 1$ if it is assumed that the initial concentration of A is 1.
(b) Derive the D-optimum design for estimating k if λ is known and the point prior for k is k^o.
(c) Now suppose that both k and λ are unknown. Show that the D_s-optimum design for λ is

$$\xi^* = \left\{ \begin{array}{cc} 0.98 & 3.33 \\ 0.43 & 0.57 \end{array} \right\}$$

if $k^o = 0.5$ and $\lambda^o = 0.5$. (Hint: Use the Equivalence Theorem for D_s-optimality.)