Q. How do dosage amount and intervals
affect the concentration of caffeine in the blood over time?

Rationale:

- This question is compelling, as its investigation can provide advice towards a proper dosage and balance of caffeine to avoid negative consequences.
- Additionally, the question of repeated doses over time is a more appropriate question than the effects of a single dose, as it more closely emulates actual behaviors.

Qualitative Model:

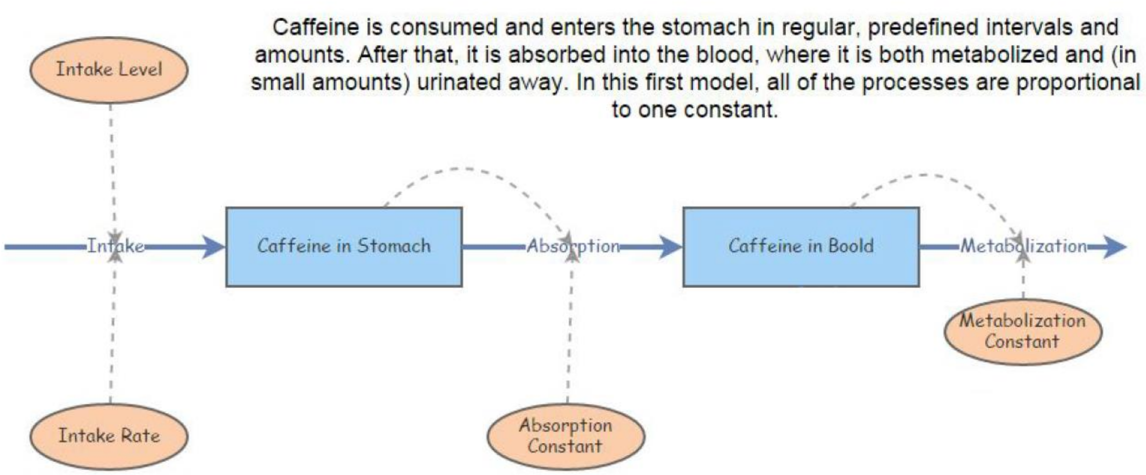


Figure 1. Stock-and-Flow Diagram of Caffeine Model.

- This model ignores caffeine absorption from the mouth, as well as gastric emptying
    - Caffeine is absorbed quite quickly (<30 minutes for peak blood concentration), so we felt that gastric emptying could be abstracted into a single absorption function.
- It also ignores the products of caffeine metabolization, as there are several that affect each other in complex ways that are outside the scope of our question
- The flows of absorption and metabolization were modeled as first order flows, as several sources suggested they would be

Quantitative Model:

- The model is structured after two differential equations, for the caffeine in the "stomach" (more accurately, the GI tract), and caffeine in the blood. Both absorption into the blood and elimination from the blood were modeled as first order functions:

$$\frac{dC_s}{dt} = -k_a C_s$$

$$\frac{dC_b}{dt} = k_a C_s - k_e C_b$$

Dosage administration was separately accounted for as a discrete intake, rather than a continuous consumption, to better model the physical world.

- Caffeine is often reported to have a half-life of 4-7 hours in the bloodstream. This number, along with the maximum time concentration from the following study, allowed us to calculate our constants
  - http://www.hindawi.com/journals/isrn/2013/147238/

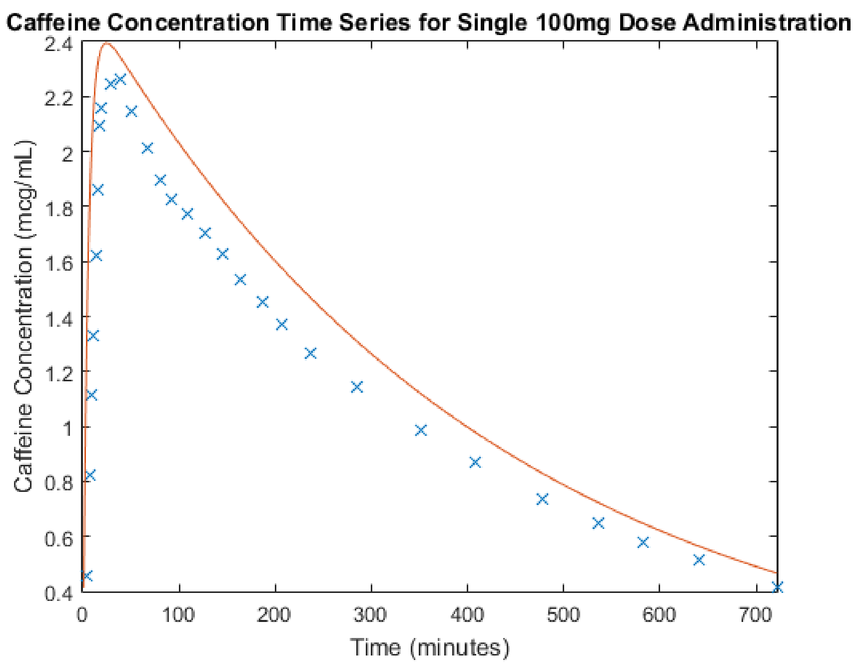


Figure 2. The comparison plot between experimental and theoretical concentration of caffeine over time.

- As shown here, our model follows the same shape of the graph with a tendency for overestimation.
  - This overestimation is not worrying, as the absorption and elimination constants can vary greatly from person to person.
- For further validation, we created a closed-form mathematical model whose behavior was found to exactly match the behavior of our simulated model:

$$\mathrm{C(t)} = C_0 * e^{-k_e t} + \frac{\frac{k_a S_0}{k_e - k_a}\left(e^{-k_a t} - e^{-k_e t}\right)}{V_d}$$

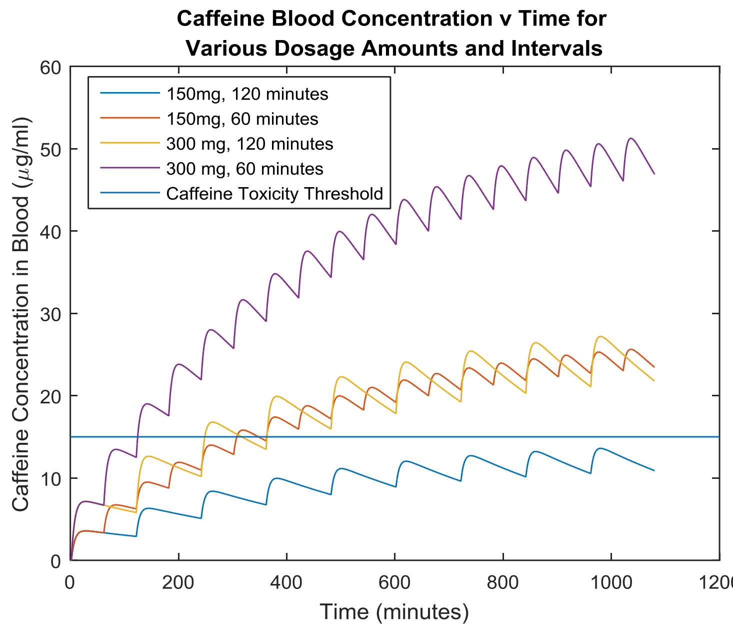
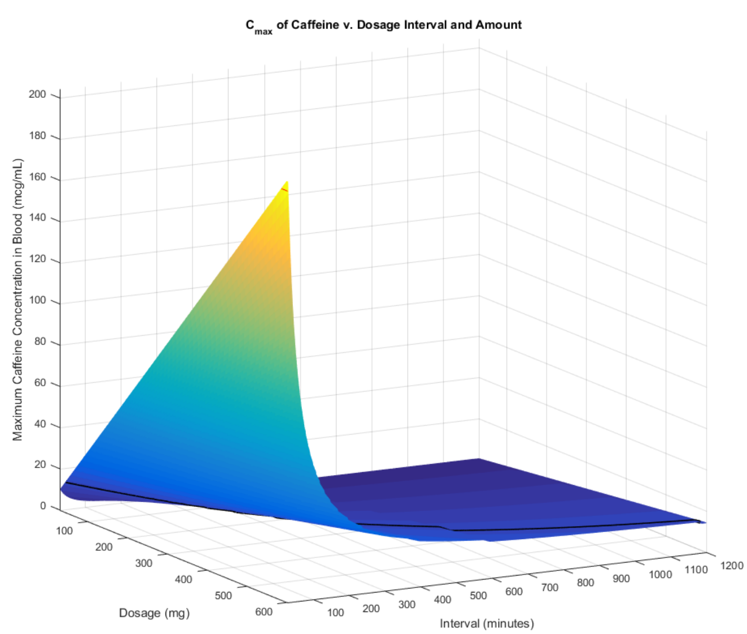
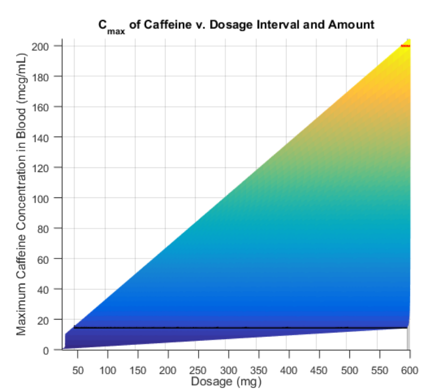
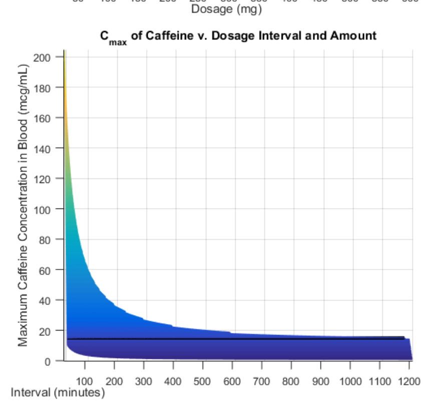


Figure 3. The time series of caffeine at various dosage amounts and intervals

- The above plot shows the effects of dosage amounts and intervals on caffeine concentration in a multiple-dose scenario. As shown, the maximum blood concentration approaches a single value over time.
- Noticing this, a 3-dimensional plot that demonstrated the relationship between maximum concentration of caffeine and the interval and amount of dosage was generated:







- The sectional observation (right) on this plot showed that the maximum concentration of caffeine was directly proportional to the amount of dosage, and (approximately) inversely proportional to the interval of dosage.
- We compared these values to the blood concentrations necessary for toxic or fatal effects of caffeine consumption; as caffeine begins to act as toxin at the concentration of 15µg/mL and reaches fatal level at 200µg/mL, the following color-coded contour plot summarizes our research:

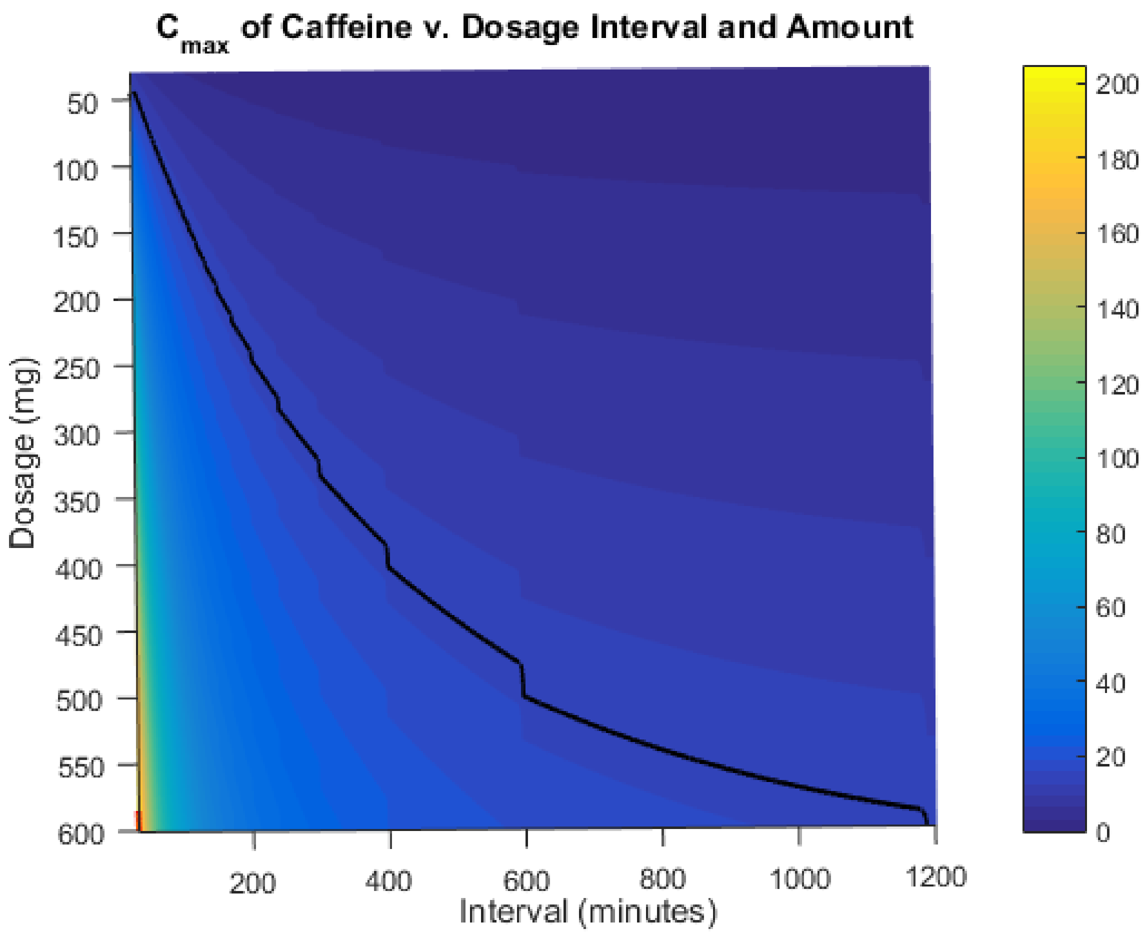


Figure 4. The maximum concentration of caffeine; the black line denotes the point at which caffeine reaches toxicity and the red a lethal concentration