White Paper – HIV Modeling with the CMS framework

**Objective:** The goal of this investigation is to determine whether the CMS team/framework could help support the modeling efforts by the HIV team. Since Dr. Anna Bershteyn has been using a deterministic ordinary differential equation model, she was the obvious contact from the HIV team since her model is fundamentally compartmental. This white paper will be a report of that interaction. The report will include a summary, action items, and conclusion.

**Summary of Meeting:** Dr. Bershteyn and I continued a discussion started before her maternity leave about the possible extensions of her model utilizing the CMS framework. Specifically, she was interested in seeing if a discrete-stochastic framework would be beneficial to the modeling work for the HIV intra-host model. There are a number of possible points where stochastic simulations may help illuminate sensitivities in the intra-host model as well as the population model when the intra-host is explicitly included in the agent-based model.

1. Modeling the dynamics with a stochastic framework might illustrate important and necessary variation that needs to be included in the intra-host model with the DTK. According to Anna, the magnitude of a few of the states of the system can become on the order of hundreds. There is the possibility that stochastic variation may be important in understanding the distribution of possible solutions for the population level models.
2. Anna is already implementing stochastic drug adherence patterns. These patterns are pre-generated via MATLAB. This could be implemented as a process in the simulation, but there was not much interest in the implementation in MATLAB.
3. A paper was recently published [1] that is very similar to Anna’s intrahost model. This work focuses on the concept of latent cells that do not begin producing virus for much longer periods of time. The CMS framework may be able to model the same phenomena, but in a stochastic modeling framework.

Anna appears to be excited about the possibility of using the framework for the intra-host model, but the current high-priority tasks associated with the modeling consortium this fall will delay this work until next year. In addition, they have not yet ported over her current intra-host model to the DTK. There is a significant amount of work that the HIV team is currently involved with and needs to be flushed out before the research described above.

**Action Items:** The following are a short list of action items for myself to help the HIV team in addition to learn more about the current literature on the HIV intra-host models.

1. Implement the intra-host model in the emodl language.
2. Investigate various drug adherence patterns to fit in the emodl language.
3. Read the new paper associated with latent HIV producing cells.

**Conclusion:** The overall impression from the meeting with Anna is that the HIV team is incredibly busy due to their upcoming deadlines. There are a few items listed above that would help the CMS team identify future needs by the HIV team. This will arrive through investigation of the new Nowak paper, [1] as well as implementing the current intra-host model.

**Citations:**

[1] Rosenbloom, et.al. “ Antiretroviral dynamics determines HIV evolution and predicts therapy outcome,” Nature Medicine 2012.