According to the World Health Organization, over 35 million people around the world are infected with the human immunodeficiency virus (HIV) and nearly half of those people are, and will be for the rest of their lives, receiving Highly Active Antiretroviral Therapy drugs (HAART). The requirement to be on these drugs for life, once infected with the virus, is based on the ability of the virus to form a latent reservoir of infected cells. HIV infects Human CD4 cells, a type of white blood cell, and integrates the RNA of the virus into the DNA of the cell. RNA, the so called “DNA of the virus,” is converted to DNA through a process called reverse transcription which is then integrated into the DNA of the CD4 cell. Spread of the infection happens when the DNA of the cell, and therefore the converted DNA from the virus too, is transcripted and translated into the RNA of the virus and the proteins carried by the virus. Together they bud off the cell as a new virus ready to infect more cells. HAART drugs can block many of the key stages of infection but they cannot eradicate cells that are infected but not producing more virus. This is known as the latent reservoir. The presence of these undetectable, infected cells means that if someone stops taking the drugs, the latent reservoir will be able to kick into action and infect more CD4 cells. Studying the timing of many of the stages along the way of infection and replication can lead to a better understanding of the virus and possibly more effective ways of reducing the progress of infection.

My research, under the supervision and guidance of professors Anding Shen (Calvin College) and Ben Holder (Grand Valley State University) attempts to understand the kinetics, or the process and timing, of the virus infection. Professor Shen also has other experiments going along the same topic of HIV infection. Work on these experiments, done by Noah Praamsma, Seth Verkaik, and volunteer Valerie Tan, often overlaps with my individual research and contributes greatly to my topic. The overall goal of the research is to provide quantitative specification regarding many factors involving infection. To do this, Professor Holder, a physics professor, uses mathematical models to simulate infections. These models require parameters established through in vitro experimentations done by Professor Shen and myself. The factors requiring quantitative specifications include the timing of infection (including the timing of reverse transcription and integration of the DNA), the fate of the cell after infection, the half-life of the virus cultured in medium, and more.

Doing this in vitro requires the drawing of blood from healthy donors and then the subsequent isolation of CD4 cells from within that blood. Culturing these cells with endothelial cells, the cells that line our blood vessels, has shown to increase infection rates during in vitro experimentation. Thus, we set our experiments to compare the various parts of the infection we are testing between resting CD4 cells, resting CD4 cells co-cultured with endothelial cells, and activated CD4 cells. We infected these cells using a pseudotyped virus that behaves like HIV but cannot bud out and infect more cells.

My research this summer has given concrete, quantitative data to previously unknown parameters. The theory of endothelial cells boosting infections rates has been supported. Along with that, that half-life of the virus was determined to be about 7-8 hours while cultured in medium. Also the increased death rate among infected cells has been demonstrated. More work is still being done and much of that work is depending on the mathematical analysis on our collected data that is currently not yet completed.
Personally this summer has been eye opening. Not only immersing me in the immense field of biological research but also stimulating my ability to dig deeper into the scientific questions plaguing our society today. The work I have done this summer feels meaningful because it can lead to a potential eradication of a virus that has harmed and taken of the lives of many people in our world. It has been both challenging and rewarding. I owe a thank you to my professors and to Calvin College for giving me this experience.