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Modeling the Effects of HIV on the Evolution of Diseases

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DIMACS REU

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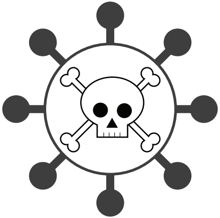
Motivating Questions

- How does the presence of HIV in the body changes the evolution of pathogens in the human body?
- How do different strains emerge at different levels of AIDS prevalence in a population?

Viruses

- Viruses are small infectious particles that can replicate only inside living cells
- Examples of viral diseases: influenza, HIV, ebola



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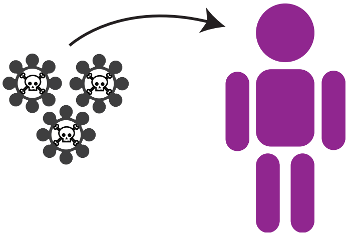

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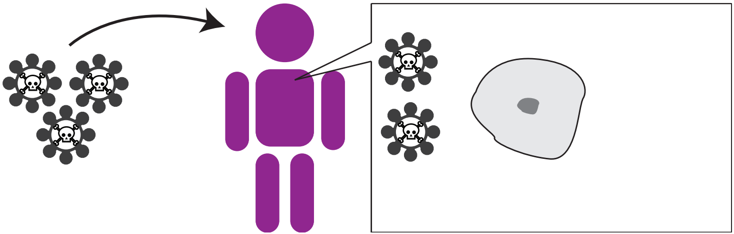

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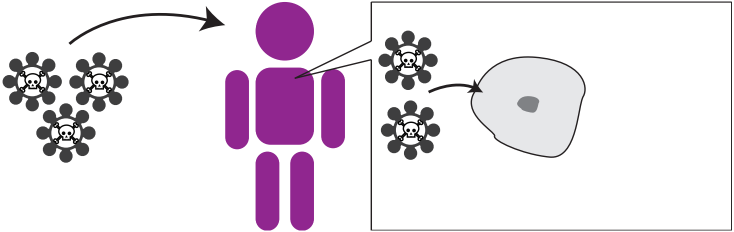

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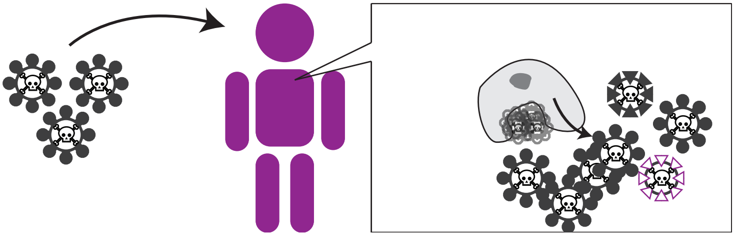

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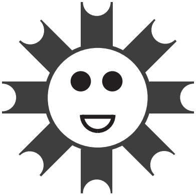
Immune Response

- A cell called *T-cells* play a big role in fighting off pathogens



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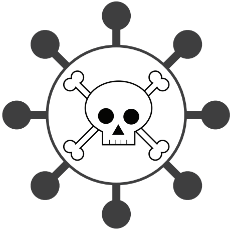

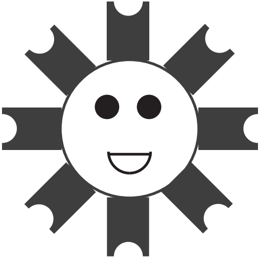

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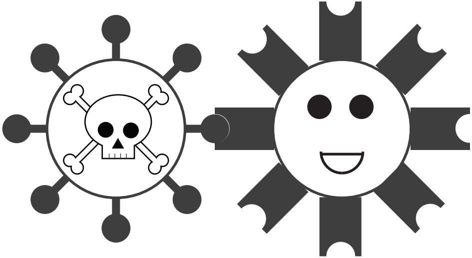

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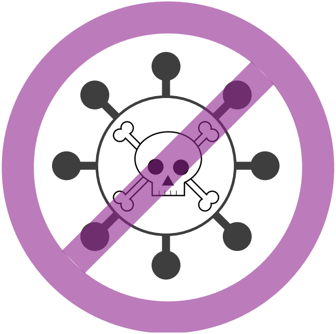

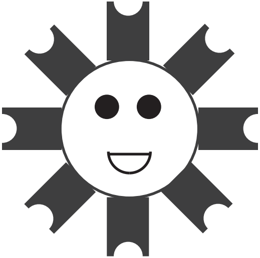

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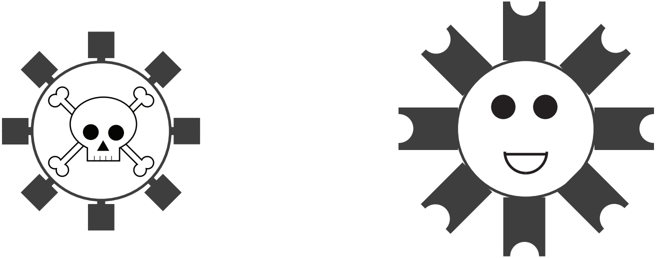

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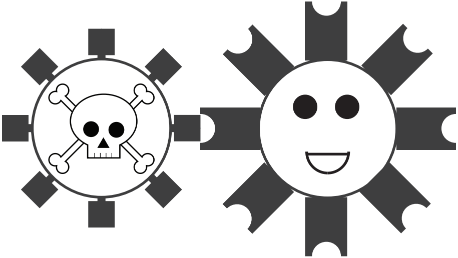

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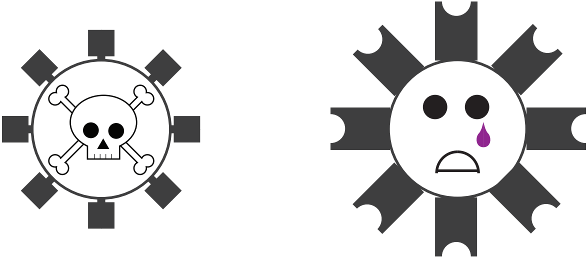
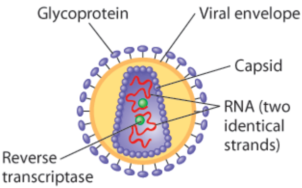


Human Immunodeficiency Virus (HIV)

- Virus that causes *acquired immunodeficiency syndrome* (AIDS)
- HIV damages the human immune system by infecting and kill T cells
  - Causes the body to lose cell-mediated immunity
  - Death due to other opportunistic infections



How are HIV and other viruses related?

- HIV/AIDS changes the evolutionary and ecological context for other diseases
- Current models exist for HIV infection and HIV strain mutations
- Very few models explore how HIV affects the evolution and mutation of *other* diseases

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Project for the Summer

- Modeling at the individual level: seeing how HIV/AIDS affects strain emergence within a person

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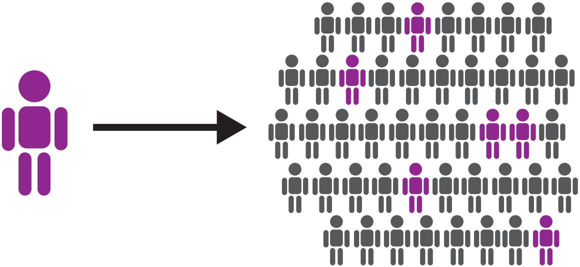
Project for the Summer

- Modeling at the individual level: seeing how HIV/AIDS affects strain emergence within a person
- Modeling at the population level: seeing how HIV/AIDS changes how strains emerge in a population



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Characteristics of the Model

- The model needs to track the evolution new strains
- In healthy individuals, the model should kill the virus
- In individuals affected with HIV/AIDS, the model should
  - Let the virus "win"
  - Let the virus grow to some intermediate level

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System of Differential Equations

- System of ODEs describes the number of virus particles of N different strains

$$\frac{ds_1}{dt} = n \cdot I(t) \ln\left(1 + \frac{r}{n}\right)\left(1 - \frac{s_1}{s_{\text{Max}}}\right) s_1 - ds_1 + \sum_{j=1}^{n} \mu_{j1} s_j - \sum_{j=1}^{n} \mu_{1j} s_1$$

$$\vdots$$

$$\frac{ds_i}{dt} = n \cdot I(t) \ln\left(1 + \frac{r}{n}\right)\left(1 - \frac{s_i}{s_{\text{Max}}}\right) s_i - ds_i + \sum_{j=1}^{n} \mu_{ji} s_j - \sum_{j=1}^{n} \mu_{ij} s_i$$

$$\vdots$$

$$\frac{ds_N}{dt} = n \cdot I(t) \ln\left(1 + \frac{r}{n}\right)\left(1 - \frac{s_N}{s_{\text{Max}}}\right) s_N - ds_N + \sum_{j=1}^{n} \mu_{jN} s_j - \sum_{j=1}^{n} \mu_{Nj} s_N$$

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Growth and Death of the Virus

$$\frac{ds_i}{dt} = I(t) \cdot \ln\left(1 + \frac{r}{n}\right)\left(1 - \frac{s_i}{s_{\text{Max}}}\right) s_i - ds_i \qquad (1)$$

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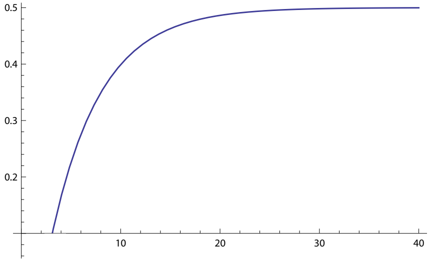
- Growth term: n number of replication cycles per day, each cycle produces r virions
  - Logistic growth term prevents unlimited growth
- Death term: Death representing the clearance of the virus by the body (e.g. lymphatic system)
- Immune response decreases the growth term

Immune Response

$$I(t) = \begin{cases} a\left(e^{-b(t-t_o)} + 1\right) & \text{if } s_i \geq \text{threshold} \\ 0 & \text{if } s_i < \text{threshold} \end{cases}$$

- Has a delay between the introduction of the virions and the immune response
- Slowly builds up to a maximal response rather than having an instantaneous maximal response



Mutation of Viruses

$$\frac{ds_i}{dt} = \sum_{j=1}^{n} \mu_{ji} s_j - \sum_{j=1}^{n} \mu_{ij} s_i$$

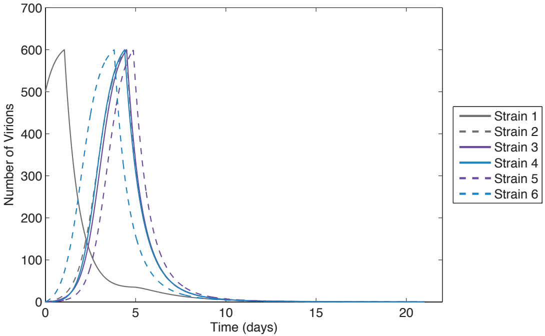
- The parameter μ_{ij} represents the rate at which strain i mutates to strain j
- For a given strain i, it can mutate to any of the other $N-1$ strains, and the other $N-1$ strains can mutate into i

$$\mu = \begin{pmatrix} 0 & \mu_{12} & & \cdots & \mu_{1n} \\ \mu_{21} & 0 & \ddots & & \\ & \ddots & \ddots & & \\ \vdots & & & & \vdots \\ \mu_{n1} & \mu_{n2} & & \cdots & \mu_{nn} \end{pmatrix}$$

Case 1: the body wins

$$\mu = \begin{pmatrix} 0 & .01 & .005 & .00004 & .002 & 0.04 \\ .0001 & 0 & 0.001 & 0.3 & .0002 & .04 \\ .0002 & 0.001 & 0 & 0.001 & .0000002 & 0 \\ 0.001 & .00002 & 0 & 0 & 0.00002 & .0000004 \\ 0.04 & 0.0003 & 0.0001 & 0.01 & 0 & 0.00001 \\ .0004 & 0.02 & 0.003 & 0.0001 & 0.005 & 0 \end{pmatrix}$$

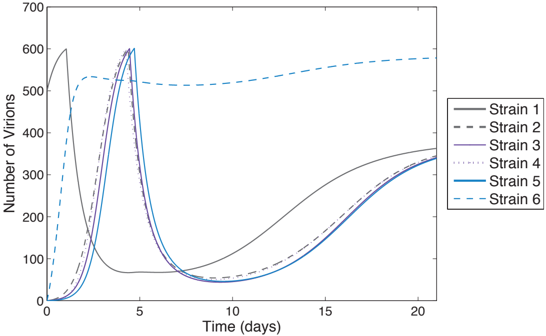
$r = 5, n = 4, d = 1.2, \text{threshold} = 600, \max I(t) = 0.3, S_1(0) = 500$



Case 2: the virus wins

$$\mu = \begin{pmatrix} 0 & .01 & .005 & .00004 & .002 & 0.4 \\ .0001 & 0 & 0.001 & 0.3 & .0002 & .04 \\ .0002 & 0.001 & 0 & 0.001 & .0000002 & 0 \\ 0.001 & .00002 & 0 & 0 & 0.00002 & .0000004 \\ 0.04 & 0.0003 & 0.0001 & 0.01 & 0 & 0.00001 \\ .0004 & 0.02 & 0.003 & 0.0001 & 0.005 & 0 \end{pmatrix}$$

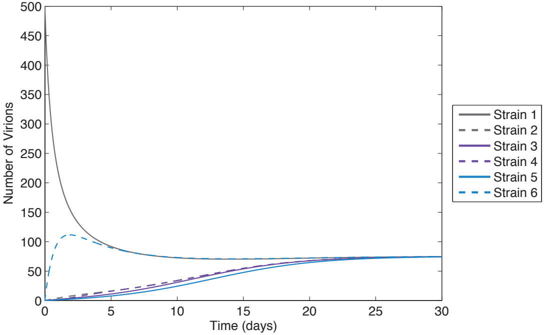
$r = 5, n = 4, d = 1.2, \text{threshold} = 600, \max I(t) = \mathbf{0.6}, S_1(0) = 500$



Case 3: nobody "wins"

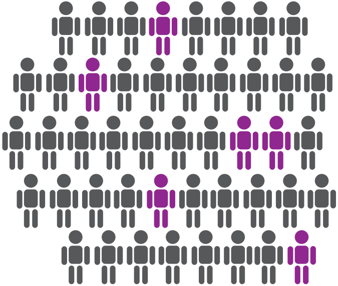
$$\mu = \begin{pmatrix} 0 & .01 & .005 & .00004 & .002 & 0.4 \\ .0001 & 0 & 0.001 & 0.3 & .0002 & .04 \\ .0002 & 0.001 & 0 & 0.001 & .0000002 & 0 \\ 0.001 & .00002 & 0 & 0 & 0.00002 & .0000004 \\ 0.04 & 0.0003 & 0.0001 & 0.01 & 0 & 0.00001 \\ .0004 & 0.02 & 0.003 & 0.0001 & 0.005 & 0 \end{pmatrix}$$

$r = 5, n = 4, \mathbf{d} = \mathbf{3}$, threshold $= 600$, $\max I(t) = 0.6$, $S_1(0) = 500$



From the Individual to the Population

- The model will be SIR-like model
- The population model will draw conclusions made in the individual model



To sum it up

- My model can demonstrates different behaviors:
  - The immune system effectively killing the virus
  - A compromised immune system losing to the virus
- These results will provide the groundwork for a population model

Future Work

- Expand the model to capture cross-immunity
- Work with different parameters, including ‘realistic’ parameter values
- Develop the population model

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Questions?