* **Evolutionary Dynamics of Viral Pathogens in Heterogeneous Host Populations**
* Model-based investigation of viral evolution in heterogeneous host populations
* Three components
  + Network
    - Node will have four/five(?) attributes: Neighbors (already included) Disease state (already included) , Currently infected strain, currently infected strain finesses(?), memory
    - Originally just start with neighbors, disease state, and currently infected strains
  + SEIR Model (eventually tie into the evolution model)
    - type of algorithm to run? chain binomial or Gillespie
  + Evolution Model
    - Neutral
    - Fitness – affects transmissibility
      * Positive – fitness gains
      * Negative –fitness losses
* Basis of Simulation
* Repeat 1000 times {
  + Generate network of size N with set characteristics (eventually put the different network conditions in here as another loop)
  + Infect one person with a random strain
  + While Number of Infected > 0 {
    - In infected individuals, mutation occurs with some probability
    - Calculate diversity, divergence measures
    - Infected individuals infect susceptible neighbors with transmission probability: (transmission might have a fitness component)
    - Go through all nodes and tally the current strains
    - Track numbers of susceptible, Infected, Recovered for each time-step
    - }
  + }
* End
* First Basic Simulation
  + Transmission doesn’t have a fitness component – parameters don’t depend on the strain/ mutations are neutral
  + There is complete cross immunity: infected once doesn’t get infected again
* Analysis:
* Keep track at each time-step of number of susceptible/infected/recovered
* Keep track of frequencies of different strains and the divergence of different strains
* Specifics I need to figure out:
  + Do I want the time-step to be the infected period?
    - If it’s not the infected period then for each time step, there is a probability that the individual strain of each infected node changes. In this case the mutation probability occurs before the transmission event.
    - What differences could this make?
  + type of algorithm to run for SIR
    - Gillespie-Stochastic algorithm (don’t want percolation, need something at each step)
    - Chain-Binomial
    - Percolation
  + Initial Sizes
    - Parameters
    - Need to scale mutation rate from prob of mutation/generation to the number of generations per time step
  + 1 season or eventually looking at two waves with migration introducing? More of a meta-population model?
* Further Complications
* Getting Started
* Options:
* EpiFire, all of the network stuff is basically there
* NetworkX-python
* EpiFire
* C++ File that creates the network and calls a simulator file
* The Simulator file contains the function where you have the SEIR model
* The evolutionary model is going to be part of the simulator file
* Incorporate the model into the simulator
* \*Looking up different ways that people incorporate molecular evolution
* Running examples in EpiFire
* $pwd
* examples/.
* $ls
* ex1\_gillespie.cpp
* MakeFile
* Ex2\_chain.cpp
* $make
* ……
* $ls
* ex1\_gillespie.cpp
* ex\_gillespie
* makefile
* (look at the ones that don’t have the .cpp)
* Lauren
* 1) DOD Scholarship
* \*writing the recommendation
* \* will have time to read the summary of goals?
* -don’t mention time at LANL in summary of goals
* -other thing to mention into Meyers does translational research with the DTRA funded project
* \*part of current research is not only asking basic questions but translating into practical tools and response for public health and defense
* 2) ARBO,
* \*read the report?
* \*overlap of the vectors, not exact, at 90%
* \* way of setting a threshold – show % threshold, number of points eliminated
* \* anything just talked to Ned about
* 3) Plan for Next Project
  + theoretical dynamic exploration of how contact structure affects diversity in the long-term
    - caroline buckee has done some, had the paper for my prelims, but I think more can be done with it (10 years ago, a lot more can be done now), came out of the santa fe complex systems summer school
  + \*looked also with meta-population models
  + Just trying to figure out how to start:
    - looking through epi-fire, running through the examples, trying to see what I'm going to modify
    - understanding the differences between chain-binomial, percolation, Gillespie algorithm
    - differences between those and how the evolution model is going to affect that
    - somehow need to incorporate a genetic sequence as some sort of state
  + Looking to see how other people have modeled evolution
    - Caroline buckee, have bits represent different strains
    - Stochasticity in the parameters
    - Allow one to reach a stable endemic level and then have another spread and see if it can establish
  + How I want to do it is based on a paper Trevor Bedford, Mercedes Pascual, and Sarah Cobey did
    - Did more of a wright-fisher process, start with N sequences and have those change
      * Each site has a probability of mutation (random switch to any of the different letters)
    - Mine won’t start with N…
  + What I think I need to do is figure out how to insert some state for each node that contains a current infection
    - Eventually want there to be cross-immunity based on current strain on also on past history
* just start with
  + pathogen
    - cpp, tutorial
    - python: network simulations
    - consider both, not too much work to write basic
* Write it out in pseudo-code
  + Specifically what question are you going to do
  + How are you going to ask it in an experimental range
  + At the end nail down exactly how you’re going to do this
* Make sure you’ve really got the literature
  + Evolutionary dynamics
  + Simulation work bit strings organisms
  + Evolutionary literature that looks at sequence evolution
    - RNA evolution sequences, projecting the secondary structure and that has a fitness function
    - How do mutations accumulate, neutral accumulate, how do mutations
  + How does evolution unfold on the frequency of mutations
* Network modeling
  + Pathogen

Parameters

* + Structure for the network, degree
  + Transmission parameters
  + Evolutionary parameters
    - Pick something simple and go from there
    - Pick an empirical system, and try to find published estimates
  + Take an exponential network
    - Evolutionary rates in HIV
  + Take those three
  + Same network (Rubella, Influenza)
* Python Kai
  + network models