FRED User's Guide

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Introduction

The accelerating growth in data availability and corresponding advances in high performance computing present new opportunities for *in silico* analysis of complex public health questions using computational modeling and simulation. FRED (A Framework for Reconstructing Epidemiological Dynamics) is an open source, modeling system developed by the University of Pittsburgh Public Health Dynamics Laboratory in collaboration with the Pittsburgh Supercomputing Center and the School of Computer Science at Carnegie Mellon University. FRED supports research on the dynamics of infectious disease epidemics, and the interacting effects of mitigation strategies, viral evolution, and personal health behavior. The system uses agent-based modeling of census-derived synthetic populations that capture the demographic and geographic distributions of the population, as well as detailed household, school, and workplace social networks. Multiple circulating and evolving strains can be simulated. Mitigation strategies in the framework include vaccination, anti-viral drugs, and school closure policies. FRED supports models of health behavior change to facilitate the study of critical personal health behaviors such as vaccine acceptance, personal hygiene and spontaneous social distancing. FRED is available through open source in the hopes of making large-scale agent-based epidemic models more useful to the policy-making and research communities, and as a teaching tool for students in public health.

History

Previous research under the Models of Infectious Disease Agent Study (MIDAS) program has shown that computer simulation models can provide ways to evaluate alternative intervention strategies for circumstances that would be infeasible to study using controlled trials. Previously, our team has used detailed census-based simulations to examine interventions in response to influenza pandemics, including vaccination policies (Lee at al, 2009, 2010a, 2011), school closure (Lee at al, 2010b; Brown et al, 2011), and the effects of commuting modalities (Cooley at al, 2011). These studies have shown that computer simulation can often reveal the relative value of competing health interventions, especially when considering novel circumstances that cannot be examined through observational or controlled studies. FRED is based largely on these previous MIDAS agent simulations, but has been completed redesigned to support rapid development of new features and a wide range of research studies.

Overview of this document

FRED is a research tool and this document is aimed at a target audience of infectious disease modelers with a high degree of computational experience. The pragmatics of obtaining, installing and running FRED have been described in the FRED QuickStart Guide. Please refer to that document for instructions, and some short tutorials. This document will describe FRED on a conceptual level. Developers will also want to consult the code-level documentation and even the code itself for specific implementation details.

Synthetic Population

For studies of regions within the United States, FRED uses the 2010 U.S. Synthetic Population Database (Version 1) from RTI International. This synthetic population uses the 2010 Decennial census and the 2007-2011 American Community Survey (ACS) as its sources of population counts and characteristics. The database contains geographically located synthetic households and household residents for the United States. This version also uses the Integrated Climate and Land Use System (ICLUS) gridded population dataset to place households across the landscape. As with past synthetic populations (Wheaton, 2012), students are assigned to schools, workers are assigned to workplaces and group quarters locations and residents are included. The 2010 U.S. Synthetic Population Ver. 1 QuickStart guide contains additional information about new data sources and processing used to develop the data. The 2010 U.S. Synthetic Population Ver. 1 data can be downloaded by state or county from the download section on https://www.epimodels.org/midas/Rpubsyntdata1.do. Please contact Bill Wheaton (wdw@rti.org) for more information.

Agent Model

Agents in FRED represent individuals in a population living in a specific geographic region. For example, many of the initial studies with FRED model the population of Allegheny County surrounding Pittsburgh, Pennsylvania. The model of the population of Allegheny County includes 1,242,755 agents. Each agent has demographic information (e.g., age, date-of-birth, sex), health information (e.g., current health status, date of infection, level of symptoms, infectiousness, susceptibility), locations for social activity (household, neighborhood, and possibly school or workplaces), and health-related behaviors (e.g., probability of getting a vaccine or staying home when sick). During each simulated day, agents interact with the other agents who share the same social activity locations. If an infectious agent interacts with a susceptible agent, there is a possibility of transmitting a disease from the infected agent to the susceptible agent. FRED simulates the population of agents during a period of time, usually several months, and tracks the spread of disease among the population. Since each infection event is recorded, it is possible to analyze the course of an infection through the population, and to evaluate several possible control measures.

The main program is contained in Fred.cc. For further details about the representation of individual agents, see files: Person.cc, Population.cc.

Demographics

The population input file specifies the sex, the age (in years), the marital status, and the profession of each agent. By default, these demographic features remain constant during a simulation run. FRED agents are given a random birthday such that the age in years agrees with the age listed in the population input file.

FRED also supports dynamic demographics: aging, births and deaths. These optional features are controlled by the parameters <code>enable_aging</code>, <code>enable_births</code>, and <code>enable_deaths</code>, respectively. If aging is enabled, then an agent's age increases on each birthday. If births are enabled, then each female of child-bearing age may become pregnant on any simulation day using age-specific maternity rates provided in the <code>yearly_maternity_rate_file</code>. Upon becoming pregnant, the agent is assigned a due-date based on a Gaussian distribution with a mean of 280 days and a standard deviation of 7 days. When the due-date arrives, the mother gives birth to a new agent who is assigned a random sex and is assigned to the same household as the mother. If death is enabled, then on each agent's birthday, it is decided whether that agent will die during the coming year using age-specific mortality rates provided in the <code>yearly_mortality_rate_file</code>. When an agent dies, it is removed from the population. For further details, see the source file <code>Demographics.cc</code>.

Health

Each agent maintains a list of current infections (one for each disease). An infection follows a natural history (e.g., latent period, infectious period, symptomatic period, as well as infectiousness) as specified via input parameters. Agent's health information also includes disease status (S, E, I, R), immunity, at-risk status, susceptibility, current symptom levels, and how many others have been infected by this agent. See Health.cc for further details.

Activities

An agent follows a daily pattern of interactions with groups of other agents. All interactions in FRED occur in a specific place. The types of places in FRED include: Households, Neighborhoods, School, Classrooms, Workplaces and Offices. Classrooms are small mixing groups with a given School. Offices are smaller mixing groups with Workplaces. Each agent maintains list of "favorite places", at most one for each of the above types. Agent may have undefined favorite places if they do not participate in that activity. For example, adults do not have a defined School or Classroom. On a typical day, the agent interacts with other agents in each favorite place that is defined.

Neighborhoods are defined on a grid with 1 km square cells. The agent's home neighborhood is the cell in which its household is located.

However, an agent may visit another neighborhood in the community during a given day. The decision about where to spend the neighborhood activity period is made independently each day, with the highest probability to visit the home neighborhood, and a lesser probability to visit one of the surrounding neighborhoods, and a small probability of visiting a randomly selected neighborhood within a given community radius.

If an agent is infectious, then any location the agent visits during that day is considered an infectious location. Susceptible agents can only become infected at an infectious location, so interactions among agents at non-infectious locations need not be simulated.

Schools are closed on weekends and during scheduled summer holidays. Schools may also be closed due to school closure policies. Students do not visit their school when the school is closed.

Similarly, most workers do not visit their workplaces on weekends. However, some workers are designated as weekend workers, and they continue to visit workplaces on weekends.

To reflect weekend schedules of schools and workplaces, the number of neighborhood contacts is increased by 50% on weekends.

See Activities.cc for more details.

Behaviors

FRED can be extended to include any number of health-related behaviors with minimal programming effort. Each behavior involves a decision on the willingness of the agent to perform the behavior. The current set of behaviors includes:

- 1. **Stay home when sick**: If an adult is symptomatic, is that person willing to stay home? If so, the agent withdraws to the household, does not interact with other in the neighborhood, at work or at school. The agent also does not begin new overnight travel.
- 2. **Keep child home when sick**: If a child is symptomatic, is the child's adult decision-maker willing to have the child withdraw to the household. In this case, the same restrictions on contact apply as in the adult "stay at home when sick" behavior.
- 3. Accept vaccine: Is an adult willing to accept a vaccine, if one is available?
- 4. Accept vaccine for child: This is the adult's willingness to have a child vaccinated.
- 5. **Accept another vaccine dose**: If a vaccine requires more than one dose, is the agent willing to accept an additional dose?
- 6. Accept another vaccine does for child: Same as above, but the decision is made by an adult on behalf of a child.

Future behaviors may include: wearing a face mask; taking anti-viral prophylaxis; staying home when well; keeping children home when well; avoiding travel; avoiding neighborhood contacts; hand-washing; and others.

Adult Decision-makers for Children

The FRED synthetic population includes information giving the relationship of each member of the household to the Householder (typically, the owner of the house or the head of the household.) This information is used to assign an adult in the household as the responsible decision-maker for the health-related behaviors of each child in the household. The rules for selecting the adult decision-maker for each child are as follows:

1. If the Householder is the parent (natural parent, adoptive parent, step-parent) of the child, then the Householder is designated the child's decision-maker.

- 2. If the Householder is the grandparent of the child and there is an adult in the householder who is a child of the Householder, then the first such adult is designated as the decision-maker for the child. Note that the household relationship data does not provide enough information to determine whether such an adult is actually the parent of the child in question.
- 3. If the Householder is the grandparent of the child and no plausible adult parent is present in the household, then the Householder is designated the decision-maker for the child.
- 4. Otherwise, a random adult in the household is designated as the decision-maker for the child.

The rules above permit multiple decision-makers per household. No preference is made on the basis of sex or age, other than that each decision-maker is an adult (i.e., at least 18 years old.)

Behavior Strategies

How real people make health decisions is an active area of research without an obvious consensus theory. Indeed, it seems likely that different people use different methods to come to decisions about health-related behavior. FRED agents can apply a variety of strategies to determine their willingness to adopt a given behavior. Each agent may revisit its willingness to perform the given behavior. Thus each strategy specification includes a frequency parameter that determines how often agents make decisions about their willingness to perform the behavior.

- 1. **Refuse**: Agent is never willing to perform the given behavior.
- 2. Accept: Agent is always willing to perform the given behavior.
- 3. **Flip Behavior**: Agent is assigned a fixed probability *p* of being willing to perform the given behavior. The agent revisits its willingness to perform the behavior according to the frequency parameter.
- 4. **Imitate Prevalence**: The agent is assigned an initial probability *p* of being willing to perform the given behavior. The agent revisits its willingness to perform the behavior according to the frequency parameter. When reconsidering the decision, the agent estimates the prevalence of willingness among the agents in its social networks: household, neighborhood, school and workplace. The estimate is a weighted average of the actual prevalence in each group. Given the weighted estimate, the agent adjusts its probability *p* toward the perceived prevalence. For example, if the agent perceives that the prevalence of willingness is 0.75, then it adjusts its own probability to be closer to 0.75.
- 5. Imitate Consensus: This strategy is similar to the Imitate Prevalence except that if the weighted estimate of prevalence exceeds a threshold, the agent adjusts its probability p toward 1; otherwise the agent adjusts its probability toward 0. For example, if the agent's threshold is 0.5, then if the agent perceives that the majority of its associates are willing to perform the behavior then the agent becomes more likely to accept the behavior; otherwise the agent becomes more likely to refuse the behavior.
- 6. **Imitate by Count**: This strategy is similar to the Imitate Consensus except that if the weighted number of nearby agents exceeds a threshold, the agent adjusts its probability *p* toward 1; otherwise the agents adjusts its probability toward 0. For example, if the agent's threshold is 3.0, then if the agent perceives that at least three of its associates is willing to perform the behavior then the agent becomes more likely to accept the behavior; otherwise the agent becomes more likely to refuse the behavior.
- 7. **Health Belief Model**: According to the Health Belief Model, people make health behavior decisions based on several specific considerations: susceptibility, severity, benefits, and barriers.
 - 1. *Perceived Susceptibility* refers to the person's estimate of how likely he or she is to become adversely affected by the disease or condition;
 - 2. Perceived Severity refers to the level of adverse consequences that are perceived to be likely if the person become affected;
 - 3. Perceived Benefits refers to the estimated protective effects of the behavior;

4. *Perceived Barriers* refers to the conditions that may prevent the agent from performing the behavior.

These constructs are clearly specific to the particular health behavior under consideration, so including an HBM strategy for a particular behavior in FRED requires customized programming. However, once the perceptions are computed, they can be combined into a decision rule using formulas developed by David Durham (Durham, 2010). These formulas have been implemented in the FRED Behavior module, and are controlled by run-time parameters. (See Parameters Section.)

Each agent is assigned a strategy independently for each behavior defined for that agent.

Population-Level Market Shares

For each behavior in FRED, the user may specify the fraction of the population using each strategy for that behavior. For example, it might be desirable to investigate the effect of varying the fraction of the population using the **Accept**, **Refuse**, and **Imitate Consensus** strategies. The user can specify a given distribution, for example, 20% of the population adopts the **Accept** strategy, 30% adopts the **Refuse** strategy, and 50% adopt the **Imitate Consensus** strategy for a given behavior. The share of the population can be specified separately for each behavior.

See files Behavior.cc, Health_Belief_Model.cc and Random_Behavior_Model.cc for further details.

Place Model

All infections in FRED are transmitted from one agent to another in some particular place. The types of places in FRED include: Households, Neighborhoods, School, Classrooms, Workplaces and Offices. The synthetic population files specify the households, school and workplaces in the modeled region. Neighborhoods, classrooms, and office are created by FRED using the methods described below.

Neighborhoods are defined on a grid with 1 km square cells. The agent's home neighborhood is the cell in which its household is located. However, an agent may visit another neighborhood in the community during a given day. (See Agent Model section.)

Classrooms are small mixing groups with a given school. Classrooms are defined by dividing up all the students who attend a given school into separate age groups. Each age group is divided into classroom groups of up to 40 students. A student interacts with the students assigned to the same classroom for the entire school year. A student also interacts (with a separate probability) with all the students attending the same school.

Offices are small mixing groups with a given workplace. Offices are defined by dividing up all the workers in a given workplace groups of up to 50 workers. A worker interacts with the other workers in the same office, and, with a separate rate, with all workers in the same workplace.

School and classrooms are closed on weekends, during scheduled summer breaks, and possibly due to school closure policies.

For further details, see files: Place_List.cc, Place.cc, Household.cc, Neighborhood.cc, School.cc, Classroom.cc, Workplace.cc, Office.cc.

Disease Model

FRED supports multiple diseases circulating in the same population. Each Disease has separate parameters specifying transmissibility, mortality rate, its natural history (e.g., latent period, infectious period, symptomatic period). See Disease.cc

Each disease has an associated Epidemic object that keeps track of population level statistics associated with the disease, such as the number of agents that are Susceptible, Exposed, Infectious and Recovered. The Epidemic object prints out the daily reports to the output file. See Epidemic.cc.

Transmission Model

The core phenomenon of an epidemic in FRED is the spread of an infection from one agent to another in a particular place. Each type of place represents a distinct environment for the spread of infection. Each type of place is characterized by two sets of numeric parameters:

- the number of contacts per infectious person per day, and
- the probability that a contact transmits an infection

The number of contacts per day for each type of place is a tunable parameter, and is set through the process described in the Calibration Section.

The transmission probability for a give place type generally depends on the age of the infectious person and the susceptible person. These are specified as vector input parameters.

The key method implementing infection is called Place::spread_infection() in Place.cc. This method is called once a day for each infectious place (having at least one infectious visitor). The method follows the following procedure:

```
For each infectious person i, the expected number of contacts is:
    Num_contacts(i) = Trans(D) * CR(P) * Inf(i) * S(P)/N(P)
    where:
        Trans(D) = the transmissibility factor for disease D,
        CR(P) = the contact rate for place P,
        Inf(i) = the infectivity of agent i,
        S(P) = the number of susceptible agents visiting place P, and
        N(P) = the number of total agents who usually visit place P
For contact number 1 .. Num_contacts(i)
    pick a susceptible agent j from today's visitors;
    let PROB = Trans_prob(i.j) \ Sus(j)
    where
        Trans_prob(i.j) = the transmission probability from i to j, and
        Sus(j) = the susceptibility of agent j.
        If a random number R is less than PROB, then agent i infects agent j.
```

For further details, see Place.cc, Household.cc

Pandemic influenza model parameterization

FRED is parameterized for a default pandemic influenza strain following the process described in (Cooley P, Brown S, Cajka J, Chasteen B, Ganapathi L, Grefenstette J, Hollingsworth CR, Lee BY, Levine B, Wheaton WD, Wagener DK. The Role of Subway Travel in an Influenza Epidemic: A New York City Simulation. J Urban Health. 2011 Aug 9. [Epub ahead of print] PubMed PMID: 21826584.) Paraphrasing the Supplementary Material from (Cooley et al. 2011):

The pandemic was assumed to have the age-dependent attack rate pattern of the historical 1957-8 "Asian" influenza A (H2N2), see Longini et al. Accordingly, we calibrated our model using the Ferguson et al. approach from historical (1957-58, 1968-69) influenza pandemics. We specifically used the 30-70 rule developed by Ferguson et al. in which 70% of all transmission occurred outside the household: 33% in the general community and 37% in schools and workplaces.

Following (Cooley et al, 2011), we adopted that additional requirement that transmission rates in schools are double those in workplaces. Calibrating the model involved targeting an epidemic with a 33% attack rate (AR) consistent with the age specific parameters derived from the 1957-58 pandemic. Daily contact rates were treated as endogenous parameters and were interpreted as the daily contact rates that reproduced a pandemic with a 33% AR in a population with no acquired immunity and satisfied the 30-70 rule. Therefore, our estimated contact patterns produced an epidemic designed to be similar in transmissibility to the 1957-58 epidemic with an AR of 33% and a basic reproductive rate (R0) of approximately 1.4.

By default, the contact rates for classrooms are double those for the school in general. Likewise, the contact rates for offices are double those for workplaces in general. These heuristic are based on the idea that individuals sustain more contacts within their smaller mixing groups at school and at work.

As in (Cooley et al, 2011) we assumed that 50% of sick individual stay at home and do not interact with anyone outside of the household. Note that our default school absentee rate is generally lower than other models (e.g., Ferguson et al. use a 90% absentee rate). Additionally, we assumed that all community contacts increase by 50% on weekends.

Contacts within Household

Calibration to the 30-70 target criteria was impossible unless within household contacts were treated differently than other locations. Following (Cooley at al, 2011), we assumed that each pair of agents within a household make contact each day with a specified probability. This probability is tuned as part of the calibration step to achieve the 30-70 target distribution.

Interventions

Vaccines

FRED provides a fairly robust capability for simulating the use of vaccines during a pandemic. Multiple vaccines can be simulated simultaneously, with differing administration schedules and target groups, and with different efficacies. Each vaccine can also have multiple doses and be restricted by age. It is also possible to model varied vaccines schedules by day. Prioritization by age groups, or by ACIP recommendation is available with the capability to vaccinate only the priority group. Currently, vaccines can only be applied to one disease.

Vaccines in FRED are currently modeled as so-called "all or nothing" vaccines. Each vaccine is given an age-specific efficacy and efficacy delay. When an agent takes a vaccine, there is a random draw to determine whether the vaccine will be efficacious for that agent. If it is not, then the vaccine has no effect until another vaccine or dose is administered. If the vaccine dose is efficacious, then the agent will become immune to the disease after the specified efficacy delay. As in real life, the agent has no knowledge as to whether their dose of vaccine was efficacious, and so if they are exposed after a failed vaccine or during the delay period, they may get sick from the disease.

Vaccination programs currently implemented can be thought of as mass vaccination strategies. At the beginning of the simulation, a set of queues is set up based on prioritization of the agents. These queues are then randomized and as vaccines are put into the system, agents can choose whether or not to accept a vaccine. To determine this decision, the simulation can use a straight coverage probability, or a more complex behavioral model. Heads of households can make decisions for younger members.

Antiviral drugs

FRED provides the ability to simulate the use of antivirals. Use of multiple antivirals can be modeled simultaneously. Modifiable antiviral characteristics include the length of antiviral treatment, the reduction in infectivity and susceptibility due to treatment, the efficacy of the antiviral, the amount of antiviral initially and currently available, and the start date for administration. The stock of an antiviral may be increased daily. Viral evolution can change the efficacy of an antiviral. Antivirals can modify the infectivity, susceptibility, and symptomaticity of an agent (through that agent's Health). Antivirals have distribution policies that determine to whom they are given. An antiviral may be designated as being used for prophylaxis.

School closure

FRED includes two school closure policies: global and individual. There are two triggers for the global school closure policy (school_closure_policy = global). First, all schools decide to close on the simulation day specified by the parameter school_closure_day, unless that parameter is negative. Second, all schools decide to close if the population attack rate exceeds a threshold (school_closure_threshold). With either trigger, school closure is delayed by a number of days indicated by the parameter school_closure_delay. Schools reopen after a number of days indicated by the parameter school closure period.

If the individual school closure policy is selected (school_closure_policy = individual), then the parameters for the attack rate used as threshold (school_closure_threshold), delay (school_closure_delay), and reopen (school_closure_period) are used as for global closure. Schools may close again if the school attack rate exceeds the threshold.

The default is no school closure policy: school_closure_policy = none

School are always closed on weekends. All schools also close for the summer if the parameter school_summer_schedule is set. In that case, schools are closed between the dates specified by parameters school_summer_start and school_summer_end, inclusive.

For details, see School.cc.

Future Interventions

It is planned to include other interventions in FRED, including: quarantine; travel restrictions; environmental interventions (e.g., vector control); behavioral changes; official announcements and warnings; and education campaigns.

Geography and Travel

FRED represents geography as a hierarchy of fixed square grids. Currently there are three layers in the hierarchy, called Large Grid, Grid, and Small Grid.

The Large Grid consists of 20km x 20km cells by default. The Large Grid is an aligned global geo-coordinate system. Cells in the Large Grid store the population count for the cell, along with a vector of all persons residing in that cell. The Large Grid can also be used to store climate or other environmental profiles (see **Seasonality** below).

The medium grid, called Grid, consists of 1km x 1km cells by default. These cells function as neighborhood units, and store information about the preferred schools and workplaces attended by people living with the cells. This information is used when agents need to change schools, or leave school and start to work.

The Small Grid consists of 10m x 10m cells. In the future, these cells will store fine-resolution information like the number of mosquitoes and the presence of water containers.

```
For further details, see source files: Large_Grid.cc, Large_Cell.cc, Grid.cc, Cell.cc, Small_Grid.cc, Small_Cell.cc.
```

As an optional feature, agents can travel overnight for one or more days. When an agent is on overnight travel, the traveling agent (called the "visitor") resides in the household associated with another agent (called the "visited agent"). The visitor interacts with agents in the visited agent's household and neighborhood. If the visitor is employed, then the visitor also interacts with the visited agent's office and workplace. Visitors do not attend school while traveling.

If travel is enabled, two additional input files are required, a cell population file and a trip list file. The cell population file contains the total population for each cell, considering the entire U.S. population. The trip list file contains a large sample of trips from one cell to another. This file covers the entire U.S. The trip file can contain samples based on data obtained from air travel databases or from any other source considered appropriate. The current default is a sample of 5 million cell-to-cell trips based on a gravity model of travel, using the formula:

```
Prob_travel(i,j) = Pop(i) * Pop(j) / (K * Distance(i,j))
```

where Pop(i) is the total population residing in cell i (derived from the entire U.S. synthetic population), Distance(i,j) is the distance in kilometers between the center of cells i and j, and K is a normalization factor so that $Prob_tarvel(i,j)$ sums to 1.0. Given the pdf defined by the above formula, we select 5 million trips (with replacement) and store these in the trip list file.

During the Travel::setup() method, the trip list sample is read, and those trips involving the model region are retained. The number of daily trips involving the population in the model region is proportional to the fraction of the retained trips. The goal is that the expected number of overnight trips involving agents in the modeled regions remains invariant, regardless of the size of the model region.

The cell population file is used to set the probability of initiating a trip between two cells. If a trip between cells i and j is selected, it is only initiated with probability dens(i) * dens(j), where dens(i) is the fraction of the total population in cell i that actually occurs in the synthetic population for the current model region. For example, if cell i is on the border of the model region and happens to contains only 50% of the entire cell population according to the current model population, then the probability of any trip to or from cell i is reduced by 50%.

Trip duration is controlled by a variable whose values were drawn from the U.S Department of Transportation National Household Survey. See the travel_duration parameter description.

Frequency of travel of individual agents is based upon their ages. This value is also derived from the National Household Survey and is controlled by the travel_age_prob_ages and travel_age_prob_values

parameters. These parameters are used to create a mapping of age to frequency of travel. For details on the age map see Age_Map.h and Age_Map.cc.

Seasonality and Climate

It is possible to alter the transmissibility of diseases througout the simulation run. A time-series profile of seasonality values that are used to scale the disease transmissibility is specified with the parameter seasonality_timestep_file. This file allows recurring seasonal forcing patterns to be given using Month-Day calendar dates or 'simulation days'. Optionally, the seasonality multiplier may be varied over FRED's **Large Grid** layer. The format of the seasonality_timestep_file is similar to that of the multistrain_timestep_file and is described in detail below.

Seasonality vs. Climate

The Seasonality feature of FRED has two basic modes of operation: the default in which the seasonality values are interpreted simply as direct multipliers to transmissibility and another ('climate mode') in which the values in the profile are interpreted as absolute (specific) humidity and transformed according to a Disease-specific function hardcoded in the **Disease** class.

The default function found in Disease.cc is:

multiplier = exp(((seasonality_Ka * seasonality_value) + seasonality_Kb)) + seasonality_min

The parameters governing the interpretation of the values given in the seasonality_timestep_file are described under Seasonal Forcing Parameters.

Run-time Parameters

The run-time parameters for FRED are contained in two parameter files. The first file is \$FRED_HOME/input_files/params.default and contains the default values of all defined run-time parameters. This file should not be modified by the user. The second file is usually called params and contains any parameter values that override the default values. The params file must exist but it may be empty.

Both files have the same format. Lines that begin with a # character are considered comments and are ignored. Parameters with scalar values are specified with lines of the form:

```
<name> = <value>
For example:
    days = 100
    diseases = 1
    city = Pittsburgh, PA
Some parameters are vector valued, in which case the format is:
< name > = < size > v_1 v_2 ... v_size
For example:
    # cdf of trip duration in days
    travel_duration = 6 0 0.2 0.4 0.6 0.8 1.0
```

If a parameter appears more than once in a parameter file, the last setting takes precedence. If a parameter appears in both params.default and params, the value in params overrides the value in params.default.

Simulation Initialization Parameters

Table 5.1: Simulation Initialization Parameters

Parameter = <default value=""></default>	Туре	Definition and Notes
diseases = 1		
	int	The number of diseases circulating in the population. Any number of diseases is allowed. Runtime and memory required is proportional to the number of diseases.
days = 240		
	int	The number of days in a single simulation run. FRED runs for the given number of days regardless of the epidemic state (that is, FRED does not stop early if no one is currently infected.)
seed = 123456		
	int	The seed for the random number generator. The seed values for all runs of the simulation are based on the initial seed and the run number, and are independent of the number of random numbers generated in other runs.
start_date = 2012-01-02		

Parameter = <default value=""></default>	Туре	Definition and Notes
	string	Simulation start date in the format YYYY-MM-DD.
rotate_start_date = 0		
	int	Whether to rotate through 7 start dates on multiple runs
reseed_day = -1		
	int	If reseed_day > -1, start each run with the same random seed and then reset the seed at day reseed_day. The effect is that the initial days will follow the same trajectory, but the simulations will follow independent trajectories starting on reseed_day. This permits estimation of conditional variance.
enable_small_grid = 0		
	int	If set, enables the high resolution geographical grid.
use_mean_latitude = 0		
	int	If use_mean_latitude = 1, then the mean latitude in the households file is used for the planar projection from (longitude,latitude) to (x,y) coordinates. This is recommended for regions substantially North or South from the US mean latitude. If set to 0 (the default), then the mean US latitude is used.
grid_large_cell_size = :	20.0	
	float	Size of large-scale grid cells in km.
grid_cell_size = 1.0		
	float	Size of normal grid cells in km.
grid_small_cell_size =	0.1	
	float	Size of high resolution grid cells in km.

Output Control Parameters

FRED produces several output files. The level of detail can be controlled by the following parameters:

Table 5.2: Output Control Parameters

Parameter = <default value=""></default>	Туре	Definition and Notes
verbose = 1		
	int	If set, print information for monitoring system progress to the standard output. Higher values produce more output.
debug = 0		
	int	If set, print verbose debugging output to stdout. Higher values produce more output.
test = 0		
	int	If set, print test output to stdout. Higher values produce more output.

Parameter = <default value=""></default>	Туре	Definition and Notes
outdir = OUT		
	string	Directory containing the output files. If the string beings with "/" it is interpreted as an absolute path. Otherwise, it is relative to the current working directory.
tracefile = none		
	string	
track_infection_events =	= 0	
	int	If set, then a file called infections <n>.txt is created for run <n>. This file contains one line per disease transmission event, showing the id of the infector, the infectee, and various other information. The format for the infections file is: DAY DISEASE_ID HOST_ID HOST_AGE INFECTOR_ID INFECTOR_AGE PLACE_ID If track_infection_events > 1, additional data is written on each line. For further details, see: Infection.cc.</n></n>
track_age_distribution :	= 0	
	int	
track_household_distrib	ution =	- 0
	int	
<pre>track_network_stats = 0</pre>		
	int	
report_age_of_infection	= 0	
	int	
report_place_of_infection	on = 0	
	int	
report_distance_of_infe	ction =	= 0
	int	
report_presenteeism = 0		
	int	
report_county_incidence	= 0	
	int	
quality_control = 1		
	int	If set, information about the size and age distribution for the various types of places is printed out in the Log file.
print_household_location	ns = 0	

Parameter = <default value=""></default>	Туре	Definition and Notes
	int	If set, a file called households.txt is printed in the output directory with format:HOUSE_LABEL LON LAT X Y ID GRID_ROW GRID_COL GRID_HOUSE_NUMBER
rr_delay = 10		
	int	Identifies the number of days between the definition of a cohort and the reporting of that cohort's reproductive rate in the output file.
print_gaia_data = 0		
	int	If set, generates data for use by Gaia.
incremental_trace = 0		
	int	
trace_headers = 0		
	int	
output_population = 0		
	int	If set, a file containing the current population will be output periodically. See explanation below.
pop_outfile = pop_out		
	string	Name of population dump file.
output_population_date_	match =	= 01-01-*
	string	If output_population is set, dump the population on any date that matches this string. The format is DD-MM-YY, with * matching any value.

Periodic Population Dumps

If the parameter output_population = 1, then a file will be written on the start day, the end day, and on any day matching output_population_date_match parameter. The file will be a dump of the population that will be identical to the input population file, but will have additional fields for the classroom and office ids (which are both set at runtime).

Population Parameters

Parameter = <default value=""></default>	Type	Definition and Notes
synthetic_population_directory = \$FRED_HOME/populations		
	string	Location of the synthetic population files.
synthetic_population_id = 2005_2009_ver2_42003		
	string	Defaults to Allegheny County Population (RTI Ver 2).
num_demes = 1		

Parameter = <default value=""></default>	Туре	Definition and Notes
	int	Deme is a local population of people whose households are contained in the same bounded geographic region. See explanation below.
msa = none		
	string	This parameter enables the use of Metropolitan and Micropolitan Statistical Areas. See explanation below.
fips = none		
	string	If set, has highest precedence and overrides city, state and county. See explanation below.
city = none		
	string	If set, overrides state and county. Format is "name state_abbreviation".
county = none		
	string	If set, overrides state. Format is "name state_abbreviation".
state = none		
	string	The state format can be the state name or abbreviation, such as: state = New York Or state = NY.
synthetic_population_ve	rsion =	= 2005_2009_ver2
	string	The synthetic_population_version will be prepended to the FIPS code to generate the synthetic_population_id.
enable_hospitals = 0		
	int	Optional support for hospitals.
enable_group_quarters =	0	
	int	Optional support for group quarters (dormitories, barracks, etc.).
enable_local_workplace_	assignr	ment = 0
	int	If set, then all workers who have a workplace outside the location file are assigned a random workplace in the location file.
community_distance = 20		
	int	Used when deciding where to spend an agent's neighborhood time, see explanation below.
community_prob = 0.1		
	int	Used when deciding where to spend an agent's neighborhood time, see explanation below.
home_neighborhood_prob	= 0.5	
	int	Used when deciding where to spend an agent's neighborhood time, see explanation below.
enable_aging = 0		

Parameter = <default value=""></default>	Туре	Definition and Notes
	int	
enable_births = 0		
	int	If set, new agents are added to the population as births.
enable_deaths = 0		
	int	If set, agents are removed from the population based on age-specific mortality.
enable_mobility = 0		
	int	
enable_migration = 0		
	int	
yearly_mortality_rate_f	ile = r	none
	string	File of age-specific mortality rates.
yearly_mobility_rate_fi	le = no	one
	string	
yearly_birth_rate_file	= none	
	string	File of age-specific rate at which female agents give birth.
birth_rate_multiplier =	1	
	int	

The synthetic_population_id parameter is the default determinant of the population files used in FRED. The paramers FIPS code, city name, county name, and state name, if set, will override the default, in that order of precedence. That is, a FIPS code overrides a city name, which overrides county and so on. In all cases, the name is ultimately transformed into a FIPS code.

```
# For Allegheny County, PA:
    fips = 42003
# The city format is "name state_abbreviation", such as:
    city = Pittsburgh PA
# The county format is "name state_abbreviation", such as:
    county = Allegheny County PA
# The state format can be the state name or abbreviation, such as:
    state = New York
    state = NY
```

FRED defines a **deme** to be a local population of people whose households are contained in the same bounded geographic region. The synthetic_population_id is used to define demes. No Synthetic Population ID may have more than one Deme ID, but a Deme ID may contain many Synthetic Population IDs. One deme is defined by default. To create a deme with more than one contiguous county, set the synthetic_population_id to a space delimited list of population ids.

```
synthetic_population_id = 2005_2009_ver2_42003 2005_2009_ver2_42007
```

To use more than one deme, set the number of demes and set additional synthetic population ids using array notation.

```
num_demes = 2
synthetic_population_id = 2005_2009_ver2_42003
synthetic population id[1] = 2005_2009_ver2_42007
```

Only the Allegheny County population files are included in the FRED download. Additional population files must be downloaded from https://www.epimodels.org/midas/Rpubsyntdata1.do and unzipped in the populations directory.

Metropolitan and Micropolitan Statistical Areas are Core Based Statistical Areas (CBSAs) defined by the U.S. Office of Management and Budget. CBSAs consist of a central urban area or urban cluster and are contiguous regions of relatively high population density, consisting of a central county and outlying counties tightly tied to the central county by commercial and commuting patterns. Metropolitan Statistical Areas have a core city of population 50,000 or greater. Micropolitan Statistical Areas have a core city of population 10,000 to 50,000. Some area of the U.S. are not included in either a metropolitan or micropolitan statistical area. For more information and a listing of CBSA codes, see http://www.census.gov/population/metro/. FRED uses the param **msa** to indicate use of a metropolitan or micropolitan statistical area. **msa** has the highest priority of the population areas and overrides synthetic_population_id parameter, FIPS, city, county, and state. All population files for a CBSA must be copied into FRED's populations directory. For example, the CBSA for the Pittsburgh, PA region is 38300. This region is made up of 6 counties and the population files for each county must be unzipped to the appropriate sub-directories in the populations directory.

```
msa = 38300
```

When deciding where to spend an agent's *neighborhood time*, there are parameters to control the probability of selecting a random cell within the *community*, defined by the parameter <code>community_distance</code> (in km), and the probability that the agent goes to its *home neighborhood* (where the household is). Using the default parameters, 50% of the time the neighborhood is the cell surrounding the household, and 10% of the time it is a random cell within 20km of home. The other 40% are distributed uniformly in the 8 cells immediately surrounding the home cell.

School Setup Parameters

These parameters determine if agents are assigned as teachers, if schools close in the summer and for what dates, and the maximum number of students per classroom. If school_classroom_size = 0, then schools are not subdivided into classrooms.

```
# if set, then each school within the region is assigned teachers
# by recruiting workers from a nearby workplace
    assign_teachers = 1
# set to 1 if schools closed during summer
    school_summer_schedule = 0
# summer closure dates (format MM-DD)
    school_summer_start = 06-01
    school_summer_end = 08-31
# max size per classroom
    school_classroom_size = 40
```

Workplace Setup Prameters

These parameters set size of workplaces and maximum number of workers per office. If office_size = 0, then workplaces are not subdivided into offices.

```
office_size = 50
small_workplace_size = 50
medium_workplace_size = 100
large_workplace_size = 500
```

Overnight Travel Parameters

COL1 ROW1 COL2 ROW2

These parameters enable long-distance overnight travel and control duration, number of trips per day, and age related frequency of travel.

```
# enable overnight travel (optional)
    enable_travel = 0
# cdf of trip duration in days
    travel_duration = 9 0 0.2 0.4 0.6 0.67 0.74 0.81 0.9 1.0
# for travel age map
    travel_age_prob_ages = 18 0 15 16 24 25 34 35 44 45 54 55 64 65 74 75 84 85 110
    travel_age_prob_values = 9 0.05 0.12 0.10 0.30 0.17 0.14 0.07 0.05 0.00
# distance threshold for overnight trips (in km)
    min_travel_distance = 100.0
# trips per day assuming entire US population
    max_trips_per_day = 1000000
# file containing list of sample trips
    tripfile = trips.txt
The format of the tripfile is:
```

where (COL1, ROW1) give the global cell coordinates for one endpoint, and (COL2, ROW2) give the global cell coordinates for the other endpoint. The order of the endpoints in irrelevant.

file with population estimate for each large cell

The format of the cell popfile is:

```
COL1 ROW1 POP
```

where (COL1, ROW1) give the global cell coordinates for one cell and POP is the number of agents in that cell according to the overall U.S. synthetic population file.

Epidemic Initialization Parameters

These parameters contol location of primary case input files, how initial infections are selected, when in the infection trajectory the initial cases are infected, and length of delay of epidemic start. Parameters for disease 0 are illustrated below (modify for each disease as needed).

Parameter = <default value=""></default>	Туре	Definition and Notes
seed_by_age = 0		
	int	Seed by age group; select with uniform probability from age range
seed_age_lower_bound =	0	
	int	Seed by age group lower bound
seed_age_upper_bound =	120	
	int	Seed by age group upper bound
advanced_seeding = expo	sed	
	string	control how far into their infection trajectory the seeds are exposed => all seeded infections start on day 0 [DEFAULT] infectious => all seeded infections start on first infectious day random => randomly select the day in the infection trajectory exposed: <float>;infectious<float> => user-specified fraction of initially exposed/infectious seeds (e.g. "exposed:0.25;infectious:0.75")</float></float>
epidemic_offset = 0		
	string	The start of an epidemic may be delayed up to 6 days. If the value is > 6, the system will assign a random delay based on the run number.
vaccine_offset = 0		
	string	The start of vaccination may be delayed up to 6 days. If the value is > 6, the system will assign a random delay based on the run number.

Place-specific Contact Parameters

The default contacts are calibrated for Allegheny County for a 33% clinical attack rate using the bifurcating SEIR model (SEIR = 0) and the RTI VERSION 2 Synthetic Population.

```
household_contacts[0] = 0.198226
neighborhood_contacts[0] = 42.478577
school_contacts[0] = 14.320478
workplace_contacts[0] = 1.589467
classroom_contacts[0] = -1
office_contacts[0] = -1
hospital_contacts[0] = 0
# community contacts increase on weekends
   weekend_contact_rate[0] = 1.5
```

Place-specific Transmission Parameters

The following parameters determine the probability that a potentially infective contact between an infectious agent and a symptomatic agent actually results in an infection. Transmission probabilities are defined for a given group in a given type of location. Each parameter is interpreted as a square matrix with the values given in row-order. The labels associated with the rows and columns (the groups) are specified in the comments, and are defined in the class associated with the parameter. For example, the definition of elementary students is defined in School.cc. The defaults are:

```
# groups = children adults
    household_prob[0] = 4 0.6 0.3 0.3 0.4

# groups = adult_workers
    workplace_prob[0] = 1 0.0575
    office_prob[0] = 1 0.0575

# groups = patients HCWs
    hospital_prob[0] = 4 0.0 0.01 0.01 0.0575

# groups = elem_students mid_students high_students teachers
    school_prob[0] = 16 0.0435 0 0 0.0435 0 0.0375 0 0.0375 0 0.0315 0.0315
    classroom_prob[0] = 16 0.0435 0 0 0.0435 0 0.0375 0 0.0375 0 0.0375 0 0.0315 0.0315

# groups = children adults
    neighborhood_prob[0] = 4 0.0048 0.0048 0.0048 0.0048
```

Input File Parameters

FRED requires several input files to describe the population of agents and the locations they visit. Another input file specifies the number of new cases that are seeded into the population on each simulation day.

There are several other optional input files that are required only if certain features are enabled. The following table describes the input file formats and related parameters.

Table 5.3: Input File Parameters

Parameter	Туре	Definition and Notes
cell_popfile = \$FRED_	HOME/i	nput_files/cell_pop.txt

Parameter	Туре	Definition and Notes	
	string	Optional file with the initial population per 20km-grid cell Format: COL ROW POPULATION Note: Only used if enable_travel = 1	
tripfile = \$FRED_HOME/input_files/trips.txt			
	string	Optional file containing sample of trips between 20km-grid cells Format: SRC_COL SRC_ROW DEST_COL DEST_ROW Note: Only used if enable_travel = 1	
<pre>primary_cases_file[d] = \$FRED_HOME/input_files/primary_cases_schedule_0.txt (for disease 0)</pre>			
	string	Required files giving the number of primary infections to introduce for each simulation day Format: time step map (see text) Note: More extensive documentation of the extended format given below; Use Epidemic Initialization Parameters to modify seeding behavior	
<pre>vaccination_capacity_file = \$FRED_HOME/input_files/vaccination_capacity-0.txt (for vaccine 0)</pre>			
	string	Optional file giving vaccine availability Format: START_DAY NUMBER_OF_DOSES Note: The number of doses is added to the system capacity every day until the day given on the following line, or until the end of the simulation	
<pre>yearly_birth_rate_file = \$FRED_HOME/input_files/birth_rate.txt</pre>			
	string	Optional file containing age-specific birth rates for females Format: AGE BIRTH_RATE where the rate is the probability of giving birth at the given age in years. Note: Only used if enable_births = 1	
<pre>yearly_mortality_rate_file = \$FRED_HOME/input_files/mortality_rate.txt</pre>			
	string	Optional file containing age-related mortality rates Format: AGE M_RATE F_RATE where the rates are for males and females of the given age in years. Note: Only used if enable_deaths = 1	

Primary Cases File Format

The primary cases file is a required file giving the number of primary infections to introduce for each simulation day. The primary_cases_file[d] follows the *Multistrain Timestep Map* input format. The default format is:

```
#line_format
# the default 100 seeds on day zero...
0 0 100
The full format is
start end attempts [ strain [ prob [ min [ lat lon radius ] ] ] ]
```

Only the first three fields are mandatory. The first two fields give the starting and ending day, and the third field specifies the number of attempted infections per day. For each specified day we attempt to generate new cases by randomly selecting agents (with replacement) and infecting them if they are susceptible. Note that the actual number of infections may be less than the number of attempts because some selected agents may already be infected or may be immune. The process continues until the end day indicated on the same line in the file, or until the end of the simulation.

The other fields are optional, but if present, must be given in the order above. If a location is specified, then all three location fields must be present (lat, lon & radius). The radius is specified in kilometers. To disable geographic seeding either omit lat, lon & radius or give a value for radius that is greater than 40075 or less than zero.

The example below will make 100 seeding attempts of strain 0 on day 0, each with attempt probability of 1, requiring a minimum of 100 transmissions, all selected randomly from people whose households are within 100km of the specified point.

```
0 0 100 0 1 100 40.44181 -80.01278 100
```

Note: Epidemic Initialization Parameters may be used to modify seeding behavior.

Global Compile-Time Constants

MAX_NUM_DISEASES:

For optimal performance, set this to the minimum value possible. The default value allows **four diseases**. Changing this values requires recompilation.

This constant is defined in Global.h.

Disease Model Parameters

Each disease is described by the following set of parameters, indexed by the disease number d, where $d = 0, \ldots, diseases-1$. Disease number is zero-indexed.

trans[d]:

The transmissibility of disease d relative to an arbitrary baseline.

```
trans[0] = 1.0
```

symp[d]:

The probability of an infected person becoming symptomatic

```
symp[0] = 0.67
```

mortality_rate[d]:

The probability of an infected person dying (Not currently implemented)

```
mortality_rate[0] = 0.00001
```

infection_model[d]:

Either 0 or 1. Infection model 0 is a bifurcating model in which each infected agent passes through stages SEIR or SEiR, where "I" means infectious and symptomatic, and "i" means infectious but not symptomatic. Infection model 1 is a sequential model in which infected agents pass through the stages SEiIR. In any model, some stages may last for 0 days, except E, which always lasts at least 1 day.

```
infection_model[0] = 0
```

days_latent[d]:

discrete cdf for number of days between becoming exposed and becoming infectious. With the values shown in the example below, there is an 80% chance of becoming infectious 1 day after exposure and a 20% chance of becoming infectious 2 days after exposure.

```
days_latent[0] = 3 0 0.8 1.0
```

days_asymp[d]:

discrete cdf for number of days the agent is infectious but asymptomatic. With the values shown in the example below, the default setting, the agent may be asymptomatic between 3 to 6 days.

```
day_asymp[0] = 7 0.0 0.0 0.0 0.3 0.7 0.9 1.0
```

days_symp[d]:

discrete cdf for number of days the agent is infectious and symptomatic. With the values shown in the example below, the default setting, the agent may be symptomatic between 3 to 6 days.

```
day_symp[0] = 7 0.0 0.0 0.0 0.3 0.7 0.9 1.0
```

immunity_loss_rate[d]:

rate at which a person loses immunity after recovering from infection. If greater than 0.0, the number of days in state "R" is drawn from an exponential distribution with parameter 1 / immunity_loss_rate.

```
immunity loss rate[0] = 0
```

symp_infectivity[d]:

multiplier for how infective a symptomatic agent is.

```
symp_infectivity[0] = 1.0
```

asymp_infectivity[d]:

multiplier for how infective an asymptomatic agent is.

```
asymp_infectivity[0] = 0.5
```

residual_immunity_ages[d]:

```
residual_immunity_ages[0] = 0
```

residual_immunity_values[d]:

```
residual immunity values[0] = 0
```

Contact Rates

The following parameters determine the number of potentially infective daily contacts between an infectious agent and a susceptible agent in a given type of location. The default values are calibrated for Allegheny County using the bifurcating infection model (infection_model = 0).

household_contacts[d]: contact rate for households

```
household_contacts[d] = 0.19
```

neighborhood contacts[d]: contact rate for neighborhoods

```
neighborhood_contacts[0] = 42.32
```

school_contacts[d]: contact rate for schools

```
school_contacts[0] = 15.83
```

workplace_contacts[d]: contact rate for workplaces

```
workplace_contacts[0] = 1.66
```

classroom_contacts[d], office_contacts[0]:

By default, classroom contacts are double the school contacts, and office contacts are double the workplace contacts. These defaults are indicated as follows:

```
classroom_contacts[0] = -1
office contacts[0] = -1
```

These defaults can be overridden if values other than -1 are provided in the params file.

weekend_contact_rate[d]: multiplier of neighborhood contacts on weekend

The default is to increase weekend contacts by 50%:

```
weekend_contact _rate[0] = 1.5
```

Transmission Probabilities

The following parameters determine the probability that a potentially infective contact between an infectious agent and a symptomatic agent actually results in an infection. Transmission probabilities are defined for a given group in a given type of location. Each parameter is interpreted as a square matrix with the values given in row-order. The labels associated with the rows and columns (the groups) are specified in the comments, and are defined in the class associated with the parameter. For example, the definition of elementary students is defined in School.cc. The defaults are:

```
# groups = children adults
   household_prob[d] = 4 0.6 0.3 0.3 0.4
   neighborhood_prob[d] = 4 0.0048 0.0048 0.0048 0.0048
# groups = adult_workers
   workplace_prob[d] = 1 0.0575
   office_prob[d] = 1 0.0575
# groups = elem_students mid_students high_students teachers
   school_prob[d] = 16 0.0435 0 0 0 0.0375 0 0 0 0.0315 0 0 0 0.0575
   classroom_prob[d] = 16 0.0435 0 0 0 0.0375 0 0 0 0.0315 0 0 0 0 0.0575
```

Multistrain Timestep Map Format

The first line of the timestep map file specifies the format to be used.

Currently #line_format is the only supported format. Future work may allow for some type of structured (key = value) format to permit more detailed specification of seeding behavior.

Any line beginning with # is interpreted as a comment and ignored. Every other line is interpreted as a seeding instruction and expected to follow the format:

```
start end attempts [ strain [ prob [ min [ lat lon radius ] ] ] ]
```

Mandatory Fields:

The first three fields (*start*, *end*, *attempts*) are mandatory. The others are optional, but, if present, must be given in the order above.

The *start* and *end* fields are indexed from zero and can be used to specify a range of days beginning on *start* and continuing to *end* (inclusive). To specify seeding on a single day, set *start* equal to *end*.

The *attempts* field determines the number of seeding attempts for the given range of time steps. If no further fields are present, this number of individuals are randomly chosen with replacement from the entire population

and transmission of the disease is attempted. Note that sampling includes individuals who may already be infected; in this case the actual number of new seeds may be less than the number specified by *attempts*.

Optional Fields:

The *strain* field gives the numeric id of the strain to be seeded for this timestep. If the *strain* field is not given, seeds will be strain "0".

The *prob* field can be used to introduce some randomness into the number of seeding events attempted at the time step. With probability 1 - *prob* each of the attempts specified by *attempt* will be skipped.

The *min* field can be used to ensure that a minimum number of attempts actually result in transmission. If specified, individuals will continue (1000 additional times) to be selected from the population until *min* number of successful transmissions have been created. If 1000 additional selections from the population are insufficient to create the specified minimum number of transmissions, a warning is given and execution of the program continues.

The geographic area from which individuals are selected can be specified by giving the coordinates of a point (lat, lon) and a *radius* specified in kilometers. When enabled, random sampling is restricted to only those individuals whose households are located within the specified area.

Additional information on the timestep map format may be found in README_Timestep_Maps.

Seasonal Forcing Parameters:

enable_seasonality:

Enables seasonality; if used without enable_climate = 1, then the values in the seasonality timestep file are interpreted as simple multipliers to transmissibility.

Default: 0

enable_climate:

Causes the seasonality values to be interpreted as absolute humidity.

Default: 0

seasonality_timestep_file:

The seasonal forcing profile. Sample profiles are available in:

```
$FRED_HOME/input_files/seasonality_timestep
$FRED_HOME/input_files/seasonality_timestep_dateformat
```

Default: none

seasonality_multiplier_max[0]:

Disease specific constant used in calculation of transmissibility multiplier when **climate** is enabled.

Default: 1

seasonality_multiplier_min[0]:

Disease specific constant used in calculation of transmissibility multiplier when **climate** is enabled.

Default: 1

seasonality_multiplier_Ka[0]:

Disease specific constant used in calculation of transmissibility multiplier when **climate** is enabled.

Default: -180

Seasonality Timestep Map:

The sample files \$FRED_HOME/input_files/seasonality_timestep and \$FRED_HOME/input_files/seasonality_timestep_dateformat contain simple profiles for both the climate and simple seasonal forcing modes of operation. See comments within these files for more information.

IMPORTANT NOTE: The first line of the file must be "#line_format"! All subsequent lines beginning with "#" are comments.

The **Seasonality_Timestep_Map** uses FRED's date format to specify the daily seasonality multiplier values (alternatively, integer values corresponding to the days elapsed since the beginning of the simulation can be used for "start day" and "end day").

The seasonality multiplier in this file follows a simple sine wave, with a maximum on Jan. 1st and a minimimum on Jul. 1st. No claims are made regarding realism (though this is a common approximation).

Dates given in the format "mm-dd" will be recycled throughout the duration of the simulation run. It is also possible to explicity give the year (yyyy-mm-dd), however those values will not be recycled.

It is also possible to mix the various formats in the same seasonality input file. If multiple entries overlap the same simulation day, the effect is not additve: the last applicable value in the timestep file will be used.

If multiple entries are given for the same time step, but the geopgraphic coordinates are different, then the values are interpolated over the large grid (using simple nearest-neighbor interpolation).

Timestep files such as this one can be generated easily using the **R** programming language. As an example:

```
> formatted_dates = format.Date( seq.Date( as.Date("2012-01-01"), as.Date("2012-12-31"), by=1 ), "%m-%d" )
> modulated_values = ( cos( seq( 0, 2*pi, by=2*pi/365 ) ) + 1 ) / 2
> latitudes = rep( 40.440788, 366 )
> longitudes = rep( -79.960199, 366 )

> write.table(
    cbind(
        formatted_dates,
        modulated_values,
        latitudes,
        longitudes
        ) [,c(1,1:4)],
        file='seasonality-sinewave', row.names=F, col.names=F, quote=F )
```

Modification of the above code should allow easy generation of any desired seasonality profile.

Example:

```
# "start day" "end day" "seasonality multiplier" "latitude" "longitude"
01-01 01-01 1 40.440788 -79.960199
01-02 01-02 0.999925919604558 40.440788 -79.960199
01-03 01-03 0.999703700369852 40.440788 -79.960199
01-04 01-04 0.999333408144238 40.440788 -79.960199
01-05 01-05 0.998815152653293 40.440788 -79.960199
```

Disease Mitigation Parameters

School Closure Parameters:

These parameters determine policies for school closure during an epidemic.

```
# school_closure_policy = none
    school_closure_policy = global
    school_closure_policy = individual
# number of days to keep a school closed
    school_closure_period = 10
# delay after reaching any trigger before closing schools
    school_closure_delay = 2
# day to close school under global policy
    school_closure_day = 10
```

enable_vaccination:

Set this parameter to enable vaccination.

Default: 0

vaccine_tracefile:

If the value is "none" no vaccine tracefiles are produced. Otherwise, a vaccine tracefile is produced for each run in the directory given the outdir parameter. A vaccine tracefile contains one record for each agent, giving the agent's vaccination history. Vaccine tracefiles are named <code>vtrace1.txt</code>, <code>vtrace2.txt</code>, etc.

```
vaccine_trace = none
```

number_of_vaccines:

the number of types of vaccines that you would like to run in the simulation. Each vaccine in the system is required to have a set of parameters or the simulation will end in error.

Default: 0

vaccine_prioritize_acip:

Enable prioritization of vaccination by ACIP recommendations. This includes persons aged 0-24, people deemed at risk for complications for influenza (see at_risk_ages and at_risk_values keywords), pregnant women (see pregnancy_prob_ages and pregnancy_prob_values keywords), and people over age 64.

Default: 0

vaccine_prioritize_by_age:

Enables prioritization of vaccination by age group. The age groups will be defined by the two following keywords.

Default: 0

vaccine_priority_age_low:

If vaccine_prioritize_by_age is specified as 1, this specifies the lower limit of the prioritized age group inclusively.

Default: 0

vaccine_priority_age_high:

If vaccine_prioritize_by_age is specified as 1, this specifies the upper limit of the prioritized age group inclusively.

Default: 100

vaccine dose priority:

If there are multi-dose vaccines, this parameter defines prioritization of people getting multiple doses vs. people getting their first dose.

Possible values:

- 1. No Priority, first come first serve
- 2. Place people getting subsequent dose at the beginning of the queue
- 3. Mix in people getting subsequent dose with other priority vaccinations randomly
- 4. Place people getting subsequent dose at the end of the queue

Default: 0

vaccine_capacity_file:

This parameter specifies a file that defines how many agents the system has the capacity to vaccinate on a given day throughout the simulation. This may be more or less than the amount of vaccine available through production. This parameter is meant to allow the user to attenuate the system's ability to actually vaccinate people due to limitations in personnel, time and resources.

The format of this file follows a reduced Multistrain TimeStep file, with a format as follows:

Day start Capacity1

Day_change1 Capacity2

Day_change2 Capacity3

For example: If one wanted to define that for the first 3 days of the simulation, the system could vaccinate no one, then on days 4-10, it could vaccinate 10000 people per day, then dropping down to 5000 per day on day 11 through the rest of the simulation, the vaccine capacity file would look like this:

10

4 10000

11 5000

The next set of parameters need to be defined for every vaccine in the simulation, and they will all be indexed by the vaccine number they define (signified by X).

vaccine_number_of_doses[X]:

Specifies the number of doses needed for vaccine X. There needs to be a dose specification for each dose indicated, or the simulation will end in error.

Default: 1

vaccine_total_avail[X]:

Specifies the total amount of doses of vaccine X available for the entire simulation.

Default: 1000000000

vaccine additional per day[X]:

The amount of vaccine X produced each day and made available to the system. The amount of vaccine produced cannot exceed vaccine total avail[X], for the entire simulation.

Default: 1000000

vaccine_starting_day[X]:

The day to start producing vaccine X at the rate defined by vaccine additional per day[X].

Default: 0

The next set of parameters must be specified for each dose (specified by Y) of vaccine X.

vaccine_next_dosage_day[X][Y]:

Specifies the day of the dosage schedule that the next dose should be taken. For instance, if the dose Z of a vaccine is to be taken 7 days after dose Y, then this parameter for dose Y would be seven. The last dose of a vaccine is always 0.

Default: 0

vaccine_dose_efficacy_ages[X][Y] and vaccine_dose_efficacy_values[X][Y]:

These parameters specify the age map for defining the efficacy of vaccine X, dose Y. The values should be probabilities between 0 and 1 that specify the probability that a person of a certain age will become immune after taking this dose of vaccine.

Defaults:

```
vaccine_dose_efficacy_ages[0][0] = 2 0 100
vaccine_dose_efficacy_values[0][0] = 1 0.70
```

vaccine_dose_efficacy_delay_ages[X][Y] and vaccine_dose_efficacy_delay_values[X][Y]:

These parameters specify the age map for defining the delay to efficacy of vaccine X dose Y. The values should be integer numbers of days by age.

Defaults:

```
vaccine_dose_efficacy_delay_ages[0][0] = 2 0 100
vaccine_dose_efficacy_delay_values[0][0] = 1 14
```

Anti-virals parameters:

```
enable_antivirals = 0 (Default)
number_antivirals = 0 (Default)
```

Epidemic Initialization Parameters

December adefault value	Turno	Definition and Notes	
Parameter = <default value=""></default>	Туре	Definition and Notes	
seed_by_age = 0			
	int	Seed by age group; select with uniform probability from age range	
seed_age_lower_bound = 0			
	int	Seed by age group lower bound	
seed_age_upper_bound = 120			
	int	Seed by age group upper bound	
advanced_seeding = exposed			
	string	control how far into their infection trajectory the seeds are exposed => all seeded infections start on day 0 [DEFAULT] infectious => all seeded infections start on first infectious day random => randomly select the day in the infection trajectory exposed: <float>;infectious<float> => user-specified fraction of initially exposed/infectious seeds (e.g. "exposed:0.25;infectious:0.75")</float></float>	

Behavioral Parameters

For each health-related behavior, FRED requires several parameters to describe how the behavior is modeled in the population. The current set of behavior includes:

```
• stay_home_when_sick
```

- keep_child_home_when_sick
- accept_vaccine
- accept_vaccine_dose

- accept_vaccine_for_child
- accept_vaccine_dose_for_child

In the following, replace <behavior_name> with the name of the specific behavior:

```
# enable the behavior
<behavior_name>_enabled = 1
#### BEHAVIOR MARKET SEGMENTS
# BEHAVIOR STRATEGY 0 = ALWAYS REFUSE
# BEHAVIOR STRATEGY 1 = ALWAYS ACCEPT
# BEHAVIOR STRATEGY 2 = FLIP WEIGHTED COIN FOR EACH DECISION
# BEHAVIOR STRATEGY 3 = IMITATE PREVALENCE
# BEHAVIOR STRATEGY 4 = IMITATE CONSENSUS
# BEHAVIOR STRATEGY 5 = IMITATE COUNT
# BEHAVIOR STRATEGY 6 = HEALTH BELIEF MODEL
# Each distribution should add up to 100
<behavior_name>_strategy_distribution = 7 50 50 0 0 0 0 0
##### FLIP/IMITATE INITIAL PROBS AND DECISION FREQUENCY
<behavior_name>_min_prob = 0
<behavior_name>_max_prob = 1
<behavior_name>_frequency = 1
#### IMITATION THRESHOLDS
<behavior_name>_imitate_consensus_threshold = 0
<behavior_name>_imitate_count_threshold = 0
##### WEIGHTS FOR IMITATION
## ORDER IS HOUSEHOLD NEIGHBORHOOD SCHOOL WORK ALL
## Weights can be any real number.
##
<behavior_name>_imitate_prevalence_weights = 5 0 0 0 0 1
<behavior_name>_imitate_consensus_weights = 5 0 0 0 0 1
<behavior_name>_imitate_count_weights = 5 0 0 0 0 1
#### IMITATE UPDATE RATES: HOW RAIDLY TO CONFORM TO CONSULT OTHERS
<behavior_name>_imitate_prevalence_update_rate = 0.1
<behavior_name>_imitate_consensus_update_rate = 0.1
<behavior_name>_imitate_count_update_rate = 0.1
<behavior_name>_susceptibility_threshold = 2 0 0
#### HEALTH BELIEF MODEL PARAMETERS (EXPERIMENTAL)
<behavior_name>_severity_threshold = 2 0 0
<behavior_name>_benefits_threshold = 2 0 0
<behavior_name>_barriers_threshold = 2 0 0
<behavior_name>_memory_decay = 2 0 0
<behavior_name>_base_odds_ratio = 1
<behavior_name>_susceptibility_odds_ratio = 1
```

```
<behavior_name>_severity_odds_ratio = 1
<behavior_name>_benefits_odds_ratio = 1
<behavior_name>_barriers_odds_ratio = 1
```

Output file format

The outfile (called out < n > .txt for run n) contains one line for each simulation day of the run. The format of the file is:

KEY	VALUE
Day	Current day counter
Date	Calendar date associated with the simulation day, eg, 2011-01-05
WkDay	Current day of week, e.g., Wed
С	Incidence
Cs	Symptomatic incidence (Number of new symptomatic cases)
Е	Number of agents in Exposed state
1	Number of agents in Infectious state
Is	Number of Infectious agents who are symptomatic
M	Number of agents that are Immune
N	Population size
Р	Prevalence
R	Number of agents in Removed (Recovered) state
S	Number of agents in Susceptible state for this disease
ScCI	Number of schools closed
Str	Disease id
Week	Epidemiological week (1-53)
Year	Epidemiological year
AR	Attack Rate
ARs	Attack Rate Symptomatic
RR	Reproductive rate

Note: RR is the reproductive rate observed for a cohort of individuals who were exposed on the same day. The day for which the cohort is defined in given by the parameter rr_delay .

The default is: rr_delay = 10

This value means that on day 10 of the output file, the RR for the cohort exposed on day 0 is reported. On day 11, the cohort exposed on day 1 is printed and so on. The delay should be made long enough to capture all the infectees of the cohort.

Running FRED

Detailed instructions for running FRED can be found in the FRED QuickStart Guide at the end of this document.

Notes for Developers

Contributed Code

FRED is intended to be a system that evolves over time to be the varied need of researchers in the infectious disease modeling field. We hope that developers will want to modify the code and add new features. If you do develop new features and want to share with the rest of the FRED community, please consider adding it to the official FRED distribution. We are happy to discuss this in more detail.

Coding Standards

The FRED team believes that coding standards in general make for cleaner, more readable code, and may help avoid certain pitfalls. We have tried to develop FRED according to the Google code standards.

No claim is made that we have achieved complete success, but we have found the attempt helpful.

Regression Tests

FRED includes a number of regression tests that can be run after editing the code to help catch unintended changes. The \$FRED_HOME/bin directory contains some scripts to support testing FRED:

make_rt directory_name	make files for regression test
rt [-p] [directory_name]	run regression test

The test directory tree is located at \$FRED_HOME/tests. The tests for the FRED base code are located in subdirectory base. There are a few other test directories, and more will be added over time. Each test directory contains at least two files: params.test and compare. The params.test file contains the run-time parameters that test the given feature. The FRED script rt runs a few FRED simulations in the test directory, using the params.test file. The output is directed to subdirectory OUT.TEST. The rt script compares the output files in OUT.TEST with the files in subdirectory OUT.RT. The specific comparisons are up to the developer, and are found in the executable file compare, which is run by the rt script when the simulations are complete. If no errors are generated by compare, then FRED can be said to have passed this particular regression test.

NOTE: In the context of a command, % refers to a system prompt and is not part of the typed command.

The rt script takes two optional arguments:

```
% rt -p test_name
```

test_name should be the name of one of the directories in \$FRED_HOME/tests. If this argument is omitted, test_name defaults to "base".

If the -p argument is given, rt will run the test simulations in parallel. If -p is given it must be the first argument.

The rt command can be run from any directory. It will temporarily change to the test directory to run FRED, and then return to the original directory.

To create a new regression test, do the following:

1. Create a new directory in \$FRED HOME/tests: % mkdir \$FRED HOME/tests/foo

- 2. Create a params file in that directory.
- 3. Create an executable file called compare that implements whatever tests you wish to make on the resulting FRED output files in subdirectory OUT.TEST.
- 4. Run the script make_rt to create the target output file. These will be stored in subdirectory OUT.RT.

```
% make_rt foo
```

5. Test your regression test by running:

```
rt foo
rt -p foo
```

FRED QuickStart Guide

Introduction

This is the QuickStart Guide to FRED. This guide contains instructions for installing and running FRED, along with tutorials for common simulation scenarios.

System Requirements

FRED is written in C++ for UNIX-like systems. It was developed primarily using gcc v. 4.2.1 but should be compatible with any other ANSI compliant C++ compiler. FRED was developed on OS X and Linux systems and requires that the following components be installed prior to use:

- gcc
- make
- Perl
- Python
- gnuplot

FRED has also been tested on Windows running Cygwin (http://www.cygwin.com). If using Cygwin, the following installation packages are recommended:

- Development
- Editors
- Graphics
- Perl
- Python
- Shells
- X11

Obtaining FRED

The FRED source distribution is available from the University of Pittsburgh MIDAS Center of Excellence at http://www.phdl.pitt.edu. To obtain the software, first click on the Register link to create an account. You must accept the FRED License Agreement (see Appendix) to register your account. Once you have registered, log in and click on the Download menu option that will take you to the download portal. Under the Download tab, you can select a version of FRED to download. The distribution is in the form of a gzipped tar file. You can also download FRED documentation, and synthetic population files from the same web page.

Installation

NOTE: In the context of a command, % refers to a system prompt and is not part of the typed command.

Extracting the FRED tar file will create a directory called FRED in the current directory:

```
% tar -xvzf FRED-archive.tgz
x FRED/Makefile
x FRED/LICENSE
```

Environment Variables

Set the environmental variable FRED_HOME to the location of the top-level FRED directory, for example:

```
% setenv FRED_HOME $HOME/FRED
```

FRED includes a directory \$FRED_HOME/bin that contains supporting scripts, so it is recommended that you add the bin directory to your runtime path, e.g.,

```
% setenv PATH "${FRED_HOME}/bin:$PATH"
```

In the following, /path/to/FRED gives the path to the FRED top-level directory. e.g. \$HOME/FRED if you installed FRED in your home directory.

It will be convenient to add the following lines to your .profile if using bash or similar shell:

```
FRED_HOME=/path/to/FRED
PATH=$FRED_HOME/bin:$PATH
```

If using csh, add the following lines to your .cshrc file:

```
setenv FRED_HOME /path/to/FRED
setenv PATH "${FRED_HOME}/bin:$PATH"
```

The environmental variables FRED_GNUPLOT and FRED_DISPLAY_PNG are optional, and if set, enable scripts that can create and display curves associated with FRED output. Set the environmental variable FRED_GNUPLOT to the location of the gnuplot executable, if it is installed on your machine. For example,

```
setenv FRED_GNUPLOT /usr/local/bin/gnuplot
```

Set the environmental variable FRED_DISPLAY_PNG to the location of the executable that displays a PNG file on the terminal, if one is installed on your machine. The following example is for OS X:

```
setenv FRED_DISPLAY_PNG /usr/bin/open
```

For Cygwin, you might try:

```
setenv FRED_GNUPLOT /usr/bin/gnuplot
setenv FRED_DISPLAY_PNG /usr/bin/display
```

Also for Cygwin, to be able to use ImageMagick for displaying figures, you have to use the shell within the Xwindow by using the following command

```
% startxwin
```

FRED Directory Structure

The following subdirectories are under \$FRED_HOME:

bin/: contains run-time scripts to manage FRED experiments. The FRED executable is also copied here.

doc/: FRED documentation files.

input_files/: Contains the default parameters file **params.default** and example input files for various features. **These files should not be changed by the user.** If you want to modify these files, copy them to a new working directory and edit them as desired. Then add parameters to your working **params** file to point to the new input files. See **params. default** for examples.

population/: Contains synthetic population files for different regions.

src/: Contains all of the sources files for FRED.

tests/: FRED regression tests.

Compiling FRED

Once you have set your environmental variables as described above, go to the FRED directory and compile the system:

```
% cd $FRED_HOME
% make
```

This should result in the creation of an executable file called FRED in the \$FRED_HOME/bin directory.

To check your installation of FRED, run the regression test script. If there are no error messages, your installation is complete. A successful test looks something like this:

```
% rt
FRED regression test: base
run 1 ... run 2 ...
comparing results ...
cmp OUT.TEST/out1.txt OUT.RT/out1.txt
cmp OUT.TEST/out2.txt OUT.RT/out2.txt
cmp OUT.TEST/infections1.txt OUT.RT/infections1.txt
cmp OUT.TEST/infections2.txt OUT.RT/infections2.txt
regression test finished.
```

If you get error messages or reports about difference among the files, please contact us for assistance. **NOTE:** FRED's regression test is not compatible with computers with a a 32-bit architecture. Regression test runs may not be identical. However, FRED results will still be valid.

Run-time Parameters

For example:

The run-time parameters for FRED are contained in two parameter files. The first file is **\$FRED_HOME/input_files/params.default** and contains the default values of all defined run-time parameters. **This file should not be modified.** The second file is usually called **params** and contains any parameter values that override the default values. The **params** file may be empty.

Both files have the same format. Lines that begin with a "#" character are considered comments and are ignored. Parameters with scalar values are specified with lines of the form:

```
<name> = <value>
For example:
    days = 100
    diseases = 1
    popfile = pop_Alleg.txt
Some parameters are vector valued, in which case the format is:
<name> = <size> v_1 v_2 ... v_size
```

```
# cdf of trip duration in days
travel duration = 6 0 0.2 0.4 0.6 0.8 1.0
```

If a parameter appears more than once in a parameter file, the last setting takes precedence. If a parameter appears in both **params.default** and **params**, the value in **params** overrides the value in **params.default**.

Running FRED

The FRED program takes an optional command line argument, the path to and name of the run-time parameters file:

```
% FRED parameter_file_name
```

If the argument is omitted the file "params" in the current working directory is assumed.

Input and output files are described in more detail in the FRED User's Guide sections. In addition, a set of scripts is provided for managing the process of running a large number of simulations with FRED. These scripts are illustrated below and are described fully in the User's Guide Section RUNTIME MANAGEMENTS SCRIPTS.

Simulation Information Management System

There are several options for running FRED. The FRED executable is copied to the \$FRED/bin directory after each make, so you can run FRED as follows from any working directory, assuming that you have added \$FRED_HOME/bin to your path:

```
% FRED [paramfile [run_number [directory]]]
```

The arguments are optional from right to left. If all three arguments are given, FRED uses the given paramfile, runs a single replication with number "run_number", and writes output files to the given directory. The output directory is relative to the current working directory.

If the third argument is omitted, the output directory is taken from the runtime parameter "outdir", with default value OUT.

If both the second and third arguments are missing, run_number defaults to 1.

If all arguments are missing, paramfile defaults to "params".

Examples:

Using the run_fred script for multiple realizations

The **run_fred** script is provided to perform multiple realizations (runs) in a local directory. Each run uses a distinct seed for the random number generator, so the results will vary from run to run. The format is:

```
% run_fred -p paramfile -d directory -s start_run -n end_run
```

The order of the arguments doesn't matter, and all arguments have default values:

```
-p "params"
-d ""
-s 1
-n 1
```

For example, the command:

```
% run_fred -p params -d FOO -s 1 -n 3
```

translates to a set of commands:

```
% FRED params 1 FOO > FOO/LOG1
% FRED params 2 FOO > FOO/LOG2
% FRED params 3 FOO > FOO/LOG3
```

after first creating directory FOO if necessary. The run_fred script also copies the params file into the output directory, for future reference.

If -d is not specified on the command line, FRED writes output files to the output directory specified in the **outdir** runtime parameters, which defaults to **OUT**. For example, if params does not specify an output directory, then

```
% run fred -n 3
```

translates to:

```
% FRED params 1 OUT > OUT/LOG1
% FRED params 2 OUT > OUT/LOG2
% FRED params 3 OUT > OUT/LOG3
```

The random seed for each run is set based on the both the seed value in the params file and on the run number, so a collection of FRED runs can be executed in any order with the same results. For example, you should get the same results in the output directory from

```
% run_fred -n 20
as from:
    % run_fred -n 10
    % run fred -s 11 -n 20
```

FRED Runtime Management Scripts

The \$FRED_HOME/bin directory includes several commands to manage the process of running FRED jobs. Commands exist for starting FRED jobs, reporting the status of those jobs, and organizing and reporting the results files. The bin directory contains the following commands:

Command	Explanation
fred_job	runs FRED and stores all associated data in a results database
fred_AR	report on the the attack rate of a simulation
fred_clear_all_results	flush the results database
fred_delete	delete a single job from the results database
fred_jobs	show that status of all jobs in the results database
fred_plot	plot one or more curves
fred_status	report the status of a single job
fred_sweep	run a set of simulation changing the value of a variable
fred_tail	show the tail of the current output file
get_distr	show the distribution of infection locations
ch	change a parameter value in a params file
р	print out the current params file
rt	run regression test

To use these commands, set the environmental variable \$FRED_HOME to the location of your FRED distribution. Then add \$FRED_HOME/bin to your path. The following are likely to be the most useful commands when starting to use FRED.

Note: In the following commands, " [" and "] " are used to enclose key, value pairs and are not part of the typed command. Those characters are used to enclose elements of a command that are optional or may be repeated.

% fred_job [-p paramsfile] [-k key]

Run FRED with the given parameter file in a working directory created in the \$FRED_HOME/RESULTS directory, and associate the working directory with the key. If the -p option is omitted, the file "params" is assumed. If the -k option is omitted, an internally created key is generated. In either case, a < key, id> pair is printed on standard output, where < id> is the identifier of directory associated with the run (i.e. $FRED_HOME/RESULTS/JOB/<id>).$

fred_job will terminate if the user supplied key has already been used. The script sets the STATUS of the request (see fred_status below). When FRED finishes, fred_job runs stats to collect data on the output variables in the outfile.

% fred_AR -k key

Return mean and std dev of attack rate (AR) for run associated with key.

% fred_clear_all_results

Flush all the data from the results database.

```
% fred delete -k key
```

Delete a single job from the results database. Example:

```
% fred_delete -k test1
   KEY = test1 RUN = 15
   You are about to delete /Users/gref/Desktop/FRED/RESULTS/RUN/15.
   This cannot be undone.
   Proceed? yes/no [no]
   Y
   /Users/gref/Desktop/FRED/RESULTS/RUN/15 deleted
```

The -f flag forces deletion:

```
% fred_delete -f -k test1
/Users/gref/Desktop/FRED/RESULTS/RUN/15 deleted
```

% fred_jobs

Shows the status of all jobs in the results database. The dates shown for FINISHED jobs reflect the time that they finished. For example:

Create a plot of one or more of the indicated measures for the indicated job(s). The plot file (type PNG) is stored in RESULTS under the run's REPORT directory.

The order of options is ignored. Required options are:

- k job_key: Multiple jobs can be specified
- -v variable: Multiple output variables can be specified

The following are optional:

- -e include errorbars on the plot
- -f fontsize: Valid values are "small", "medium", "large" and "giant".
- -x xmin -X xmax: Limit the range of the x-axis
- -y ymin -Y xmax: Limit the range of the x-axis
- -T title: e.g, -T 'This is a\n Two Line Title'
- --clean removes the gnuplot input file and the png file
- --name prints the full path to the plot file
- --data prints the data for plotting the graph to standard output, in space delimited format:

```
day mean stdev
```

```
% fred status -k key [-s secs]
```

Print the status of the FRED run associated with the given key. If -s option is given, repeats status report every secs seconds.

```
% fred_sweep key param lower_bound upper_bound increment
```

Run a set of simulations changing the value of a parameter. All 5 arguments are required. The arguments are: key = a suffix for the parameter file that defines the scenario; param = the name of the parameter you wish to sweep; lower_bound, upper_bound, increment are self-explanatory.

You must first create a file called params.parameters. That sets up the rest of the parameters. For each value of the named parameter, the script creates a params file called params.key_<parameter>=<value> and executes the command:

```
% fred_job -p params.<key>_<parameter>=<value> -k <key>_<parameter>=<value>
```

Each fred_job command is executed in the foreground, so the jobs run one at a time.

Note If the parameter contained a shell meta-character (such as [or], you should enclose the parameter name in quotes. Example:

```
% fred_sweep baseline 'trans[0]' 0.9 1.1 0.1
```

has the effect of making three copies of the file params.baseline, changing the value of trans[0] in each one and executes

```
% fred_job -p params.baseline_trans[0]=0.9 -k baseline-trans[0]-0.9
% fred_job -p params.baseline_trans[0]=1 -k baseline-trans[0]-1
% fred_job -p params.baseline_trans[0]=1.1 -k baseline-trans[0]-1.1
```

% fred_tail -k key

Run the tail -f command on the current output file.

```
% get distr
```

Show the distribution of infection locations.

ch

```
% ch param_name value [ paramfile ]
```

Edit the given paramfile (or params if no file is given) and add a line param_name = value

First checks to see if the given param_name occurs in params.default.

% p

Print out the current params file.

% rt

Runs regression test.

Tips for Creating FRED Working Directories

Users may find it convenient to create a new working directory when experimenting with FRED. Assuming that you have created the environmental variables as described previously, FRED can be executed in any directory. The only required file is **params**, which may be empty. For convenience, you may want to copy the files in the directory \$FRED_HOME/input_files to a new FRED working directory:

```
% mkdir test
% cd test
% cp $FRED_HOME/input_files/params params.foo
```

Edit params.foo to include the desired settings.

```
% fred_job -p params.foo -k test
```

Note also that some of the files provided in \$FRED_HOME/input_files/ are specific to Allegheny County, Pennsylvania, and may need to be revised for other locations. The location specific files are:

- birth_rate.txt
- mortality_rate.txt
- seasonality_timestep

If you wish to modify any of the input files, copy them to your working directory and edit them, and then set the appropriate parameters to tell FRED to use the new files. See examples of file location parameters in **params.default**.

Tutorials

When running FRED from the command line, it is recommended that you use the scripts provided in the directory \$FRED_HOME/bin. These scripts will store all metadata associated with each job in the FRED RESULTS database. This database is currently a directory-tree stored in the directory \$FRED_HOME/RESULTS.

It is recommended that you run FRED jobs in a working directory, for example \$FRED_HOME/work.

Tutorial 1: Running a baseline epidemic for Allegheny County.

Here is a sample parameter file:

```
% cat params.baseline
days = 100
```

This will run FRED for 100 simulated days using the default influenza parameters for Allegheny County. All runtime parameters not given in the parameter file will be given default values specified in file params.default.

To execute FRED, use the command

```
% fred_job -p params.baseline -k baseline &
```

The -p argument is the parameter file and the -k argument gives a user-defined name for the job. The run will run in the background.

You can check the status of the job using the fred_status command:

```
% fred_status -k baseline
   RUNNING-00 Tue Nov 29 21:50:15 2011
% fred_status -k baseline
   FINISHED Tue Nov 29 21:52:10 2011
```

The command fred_jobs shows the status of all jobs:

When the job is finished, you can display results. The variable(s) to be display are listed after the -v flag.

```
% fred_plot -k baseline -v S -v E -v I -v R
```



% fred_plot -k baseline -v AR



% fred_plot -k baseline -v RR



You can also get the data associated with a plot:

```
% fred_plot --data -k baseline -v AR
    0 0.01 0
    1 0.01 0
    2 0.01 0
    3 0.02 0
    4 0.03 0
    5 0.03 0
    .
    .
    95 49.75 0
    96 49.75 0
```

97 49.75 0 98 49.75 0 99 49.75 0

Tutorial 2: Varying the transmission parameter

The transmissibility of disease 0 (the default disease) is indicated by the parameter trans[0], and has a default value of 1 for influenza (this is calibrated to a serological attack rate of 50%). We will define two new parameter files:

```
% cat params.weak
   days = 100
   trans[0] = 0.8
% cat params.strong
   days = 100 trans[0] = 1.2
```

Now run two FRED jobs:

```
% fred_job -p params.weak -k weak
% fred_job -p params.strong -k strong
```

The jobs can be run in parallel if you have sufficient memory (approximately 2GB per job for Allegheny County).

When the jobs are finished you can display the results. You can display multiple plots on the same graph by specifying multiple keys (with -k). The following also demonstrates the use of -Y to control the maximum value on the y-axis, and changing the font size to large:

% fred_plot -k weak -k strong -k baseline -v AR -Y 70 -f large



The following plot shows the prevalence of the three epidemics, using the plotting option --norm to normalize to counts per 100,000:

% fred_plot -k weak -k strong -k baseline -v P -f large --norm



Tutorial 3: Varying a behavioral parameter

As an example of varying the behavior of FRED agents, we will change the probability that agents stay home when sick. The default is that 50% of the agents stay home when sick. We will define two new parameter files:

```
% cat params.stay-40
   days = 100
   sick_day_prob = 0.4
% cat params.stay-60
   days = 100
   sick_day_prob = 0.6
```

The first file specifies that 40% of the agents will stay home when they have symptoms. The second file says that 60% of the agents will stay home when sick.

Now run two more FRED jobs:

```
% fred_job -p params.stay-40 -k stay-40
% fred_job -p params.stay-60 -k stay-60
```

When the jobs are finished you can display the results:

% fred_plot -v AR -k stay-40 -k stay-60 -k baseline



% fred_plot -v P -k stay-40 -k stay-60 -k baseline



Further Exercises:

Explore combinations of FRED parameters by adding additional lines to the parameter files. See the FRED Users Guide for discussions of FRED parameters.

References

Beckman RJ., Baggerly K, McKay M. Creating synthetic baseline populations. Transportation Research Part A: Policy and Practice. 1996; 30(6): 415-429.

Brown ST, Tai JH, Bailey RR, Cooley PC, Wheaton WD, Potter MA, Voorhees RE, LeJeune M, Grefenstette JJ, Burke DS, McGlone SM, Lee BY. Would school closure for the 2009 H1N1 influenza epidemic have been worth the cost?: a computational simulation of Pennsylvania. BMC Public Health. 2011 May 20;11:353. PubMed PMID: 21599920; PubMed Central PMCID: PMC3119163.

Cajka, JC, Cooley, PC, Wheaton, WD. Attribute Assignment to a Synthetic Population in Support of Agent-Based Disease Modeling RTI Press. 2010;

Cooley P, Brown S, Cajka J, Chasteen B, Ganapathi L, Grefenstette J, Hollingsworth CR, Lee BY, Levine B, Wheaton WD, Wagener DK. The role of subway travel in an influenza epidemic: a New York City simulation. J Urban Health. 2011 Oct;88(5):982-95. PubMed PMID: 21826584; PubMed Central PMCID: PMC3191213.

Lee BY, Brown ST, Cooley PC, Zimmerman RK, Wheaton WD, Zimmer SM, Grefenstette JJ, Assi TM, Furphy TJ, Wagener DK, Burke DS. A computer simulation of employee vaccination to mitigate an influenza epidemic. Am J Prev Med. 2010 Mar;38(3):247-57. Epub 2009 Dec 30. PubMed PMID: 20042311; PubMed Central PMCID: PMC2833347.

Lee BY, Brown ST, Korch GW, Cooley PC, Zimmerman RK, Wheaton WD, Zimmer SM, Grefenstette JJ, Bailey RR, Assi TM, Burke DS. A computer simulation of vaccine prioritization, allocation, and rationing during the 2009 H1N1 influenza pandemic. Vaccine. 2010 Jul 12;28(31):4875-9. Epub 2010 May 16. PubMed PMID: 20483192; PubMed Central PMCID: PMC2906666.

Lee BY, Brown ST, Cooley P, Potter MA, Wheaton WD, Voorhees RE, Stebbins S, Grefenstette JJ, Zimmer SM, Zimmerman RK, Assi TM, Bailey RR, Wagener DK, Burke DS. Simulating school closure strategies to mitigate an influenza epidemic. J Public Health Manag Pract. 2010 May-Jun;16(3):252-61. PubMed PMID: 20035236; PubMed Central PMCID: PMC2901099.

Lee BY, Brown ST, Bailey RR, Zimmerman RK, Potter MA, McGlone SM, Cooley PC, Grefenstette JJ, Zimmer SM, Wheaton WD, Quinn SC, Voorhees RE, Burke DS. The benefits to all of ensuring equal and timely access to influenza vaccines in poor communities. Health Aff (Millwood). 2011 Jun;30(6):1141-50. PubMed PMID: 21653968.

Wheaton, W.D., Cajka, J.C., Chasteen, B.M., Wagener, D.K., Cooley, P.C., Ganapathi, L., Roberts, D.J., Allpress, J.L. (May 2009). Synthesized population databases: A US geospatial database for agent-based models: RTI Press Publication No. MR-0010-0905. Research Triangle Park, NC: RTI Press.

Appendix: FRED License Agreement

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