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# 1 Overview

Modeling and simulations allow for the exploration of scenarios and events. They provide answers to questions such as 'what happens if measles vaccination rates drop below x%' and 'would mandating paid sick leave days for everyone reduce the spread of infectious diseases?

There are many types of models. Agent-based models (ABMs) model a collection of autonomous agents. ABMs (also known as individual-based models) track the actions and interactions of a population of individual agents and their environment. Each agent's characteristics and environment can influence the actions and interactions they take. Interactions between agents on large-scales can produce complex and unexpected results on the population scale. In epidemiology, agent-based models typically use humans as agents (although animals and vectors, such as mosquitoes, have also been used). Epidemiological agent-based models have been used in a range of studies, for example, evaluating the benefit of intervention strategies in epidemics [1, 2, 3, 4, 5, 6, 7, 8].

ABMs can be relatively difficult to create, as they typically require the use of a programming language. They can also require significant computational power to run. FRED Web is a simulation platform which allows ABMs to be created, simulated and analyzed without knowledge of programming and using the computational power of the FRED Web server.

# 2 The synthetic population

FRED Web uses census-based synthetic populations to populate its simulations with agents and locations. Currently synthetic populations exist for the U.S. and the Indian state of Telangana.

The U.S. population used in FRED Web matches demographic distributions to the census tract level, including age, gender, race, household size and household income and was created by RTI international [9, 10]. Simulations can be run with populations from the County level upwards (although a large amount of RAM is required to simulate populations greater than  $\sim 100$  million).

A detailed explanation of the U.S. synthetic population creation process is given by Wheaton et al. [10].

Agents are assigned households, which are usually houses with a small number of occupants, matching the distribution of family home sizes. Some agents, however, are assigned to group quarters (college dorms, prisons, military barracks and nursing homes) if such residences exist in the population area.

Agents are also assigned to workplaces or schools, depending on the employment rate, gender and age. Three-dimensional spatial coordinates (latitude, longitude and altitude) are included for each location.

School locations match US school locations. Census data is used to assign school-age (4-17) children to a public, private or home school. Public school students are assigned to their closest school within their county with available space for their grade (as measured by road distance). Private school allocation is allowed to cross county lines and is weighted by distance.

Workplace locations and sizes match census data recording the number of workers by Census tract of household and Census tract of work.

## 3 FRED

FRED Web is built upon the FRED (A Framework for Reconstructing Epidemiological Dynamics) simulation code [11]. FRED is designed to and run ABMs, using a synthetic population.

In a FRED simulation, agents move serially from their household to their workplace/school and back on each day Agents may interact with other agents at each of these locations, as well as the neighborhood surrounding their household <sup>1</sup>.

FRED was originally designed to model the spread of infectious diseases; agents who interacted in locations could infect one-another with diseases. However, the flexibility of FRED allows it to model a wide range of scenarios.

FRED tracks the condition of agents using 'Conditions'. Conditions provide a versatile framework for modeling a large range of characteristics for each agent. Any number of conditions may be used in a FRED model.

An example FRED condition to model influenza could follow an SIR model. SIR, an abbreviation of Susceptible-Infectious-Recovered, is a standard epidemiological model to describe the possible states of an infectious disease that each person in a population could occupy. All population members begin in the Susceptible state, except for a small number in the Infectious

<sup>&</sup>lt;sup>1</sup>Agents who are unemployed do not interact with other agents at a workplace or school. Most agents work Monday-Friday, although a minority work weekends. Neighborhood interactions increase 50% on weekends

state. As the Infectious people interact with people in the Susceptible states, some of the Susceptible people are infected and enter the 'Infectious' state. These new members of the Infectious state are now able to infect population members still in the Susceptible state. After a period of time in the Infectious state, people cease to be infective and move to the 'Recovered' state.

A second condition could pertain to vaccination use, with states describing whether each person has: not taken a vaccine, taken a vaccine in the past two weeks (vaccines typically take  $\sim 2$  weeks to be effective), developed immunity, or failed to develop immunity.

FRED can assign agents to conditions based on demographic characteristics, hence maternity could be modeled by separating agents into gender and age states. Female agents aged 15-20 could be declared pregnant with probability  $p_1$ , 20-25 with probability  $p_2$ , etc.

The Condition creation process will be detailed below.

# 4 Using FRED Web

FRED Web is an online interface for FRED, which provides the resources to simulate create, run and analyze models. Simulation results can used to generate plots and s, as well as downloaded as CSV files. The following tutorials will provide an introduction to using FRED Web. We will start by creating a simple model of the spread of influenza in a community. Once created, we will expand the model to allow for changes in human behavior in the form of social-distancing and vaccination behavior.

# 4.1 Registration

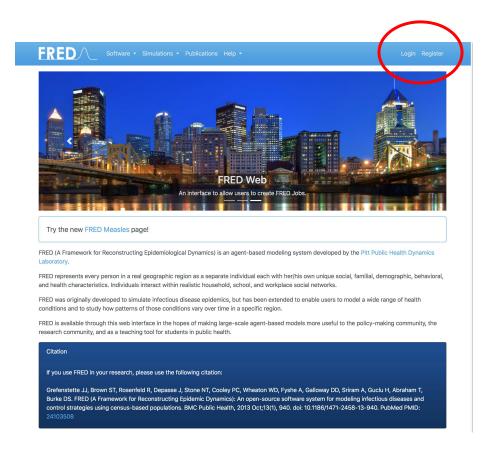


Figure 1: FRED home page

FRED Web can be accessed at http://fred.publichealth.pitt.edu. New users should *Register* using the button located in the top-right (indicated in fig. 1). Once registered, users can *Login*.

# 4.2 Project creation

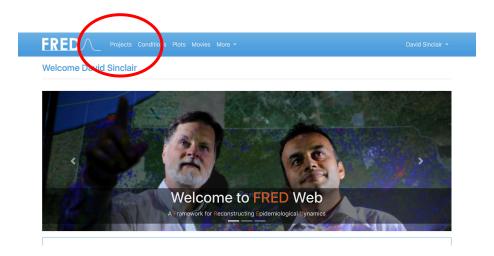


Figure 2: Accessing the *Projects* page

FRED Web lets users organize work into separate *Projects*. The *Projects* tab can be found in the top banner (indicated in fig. 2). When clicked, the user will be able to select any previously created projects, or to *Create a new project*. We will call ours, MyFirstProject, but the reader may use any name they like. After it is created, clicking on *MyFirstProject* will show a page listing the jobs (i.e. simulations) and plots associated with *MyFirstProject*. For now, they will simply say 'None'.

#### 4.3 Condition creation

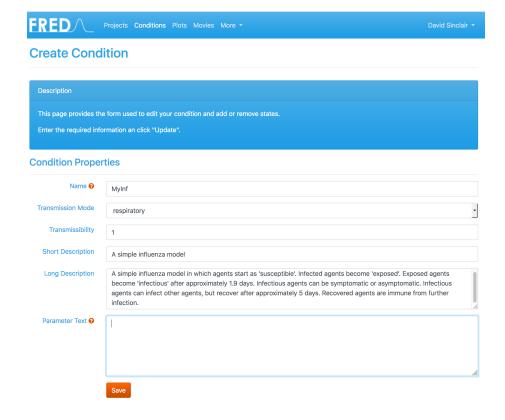


Figure 3: Condition creation

Conditions are an integral part of the FRED modeling process. Conditions can be used to affect the behavior of agents and track their health status in an epidemic. To create a condition, select the *Conditions* tab in the top banner. A list of *Shared* 

Conditions are provided, which users may include in their models. For now, however, we will create a new Condition to describe an Influenza outbreak and the subsequent impact of agents' actions. Select Create Condition to begin and enter a name (we will use MyInf). Select Transmission mode respiratory for an infectious disease spread by proximity (transmission mode proximity functions in the same way). A Transmissibility is also required to be entered; use 1 in this example. The Condition's Transmissibility affects the baseline probability that an infectious individual transmits the infection to a susceptible individual if they are in the same place at the same. The user should enter short and long explanatory descriptions of the Condition, which explains how the Condition functions. Leave the Parameter Text box empty (this is used for advanced features covered later). Your page should look similar to fig. 3. Select Save.

### 4.3.1 Creating States

The *MyInf* Condition will be created and a summary displayed. FRED Web will alert the user to add States to the Condition. To do so, select *Create State*, which opens a page with an array of options.

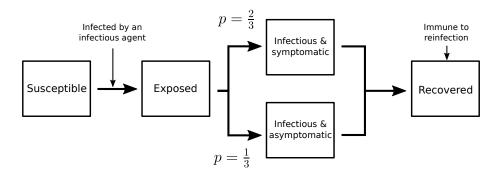


Figure 4: Susceptible-Exposed-Infectious-Recovered (SEIR) diagram for the simple influenza model

We will create an SEIR-type (Susceptible-Exposed-Infectious-Recovered) model with States in *MyInf*. As shown in fig. 4, we will deviate slightly from a classic SEIR model and allow infectious agents to be either symptomatic or asymptomatic. In our SEIR model, we want agents to remain in the susceptible state, *S*, unless they are exposed by an agent in either the infectious and symptomatic state, *Is*, or the infectious and asymptomatic state, *Ia*. On exposure, agents should enter the exposed state, *E*, for a short period, until they become either infectious and symptomatic (State: *Is*), or infectious and asymptomatic (State: *Ia*). After a period of time, infectious agents will enter the recovered state, *R*.

First we will define the States, and after we will describe how to control movement between States. Definitions of each option within a State are given in table 1.

Adjust the following inputs, leaving the other options as their default. Select Save.

Name: S

• *Exposed State:* No

• Duration Distribution: lognormal

• Duration Median: 9999

• Duration Dispersion: 1

• Susceptibility: 1

• Transmissibility: 0

Your State S should look similar to fig. 5. Create a second state and enter:

• *Name*: E

• Exposed State: Yes

• Duration Distribution: lognormal

• Duration Median: 1.9

• Duration Dispersion: 1.23

 Table 1: Create State page options

Name	Identifier for the state
Exposed State	If someone is infected with the disease, this the state they immediately enter. An example is the Exposed state, $E$ , in an SEIR model, and the Infectious state, $I$ , in an SIR model
Maternity state	If an agent enters a maternity state, a new agent will be created. The agent occupies the same house as the agent who entered the maternity state
Is Dormant	If an agent will stay in this state indefinitely, select this option to speed up the simulation time. An example would be the Recovered state, <i>R</i> , in an SIR model.
Fatal state	If an agent enters a fatal state, that agent is 'killed' and removed from the remainder of the simulation.
Duration Distribution	Distribution type to use for time an agent stays in this state (currently only lognormal available)
Duration Median	Median number of days an agent stays in this state. A value of 9999 or -1 means agents will stay in this state until an action caused by another state (i.e. become infected) causes them to move state. A value of 0 means transitions away from this State are evaluated and enacted immediately upon entering.
Duration Dispersion	Dispersion (in number of days) on the Duration Median. In a log-normal distribution, one standard deviation of a dispersion is defined as $\frac{m}{d}$ to $m \cdot d$ , where $m$ is the median and $d$ is the dispersion.
Susceptibility	If a transmission event occurs (see Transmissibility, below), susceptibility determines the probability of an agent becoming exposed. The susceptibility of an immune agent is 0.
Transmissibility	The transmissibility of a condition is multiplied by the transmissibility of a state, to give the total probability of transmission event occurring by an agent in a state.
Decide Household Confinement Daily	If agent has probability of staying home that day due to being in this state, is the household confinement determined each day, or just once on entering this state
Probability Of Household Confinement	Probability that an agent in this state will only interact with other agents in their household. Works with <i>Decide Household Confinement Daily</i>
Probability Absent From Work	Probability that an agent in this state will not attend work (but interact with agents in other aspects of their daily routine, e.g. agents in their neighborhood)
Probability Absent From School	Probability that an agent in this state will not attend school (but interact with agents in other aspects of their daily routine, e.g. agents in their neighborhood)
Probability Absent From Neighborhood	Probability that an agent in this state will not interact with other agents in their neighborhood (but interact with agents in other aspects of their daily routine, e.g. their workplace or school)
Probability Of Isolation	Probability that an agent in this state will not interact with any other agent, including their household.

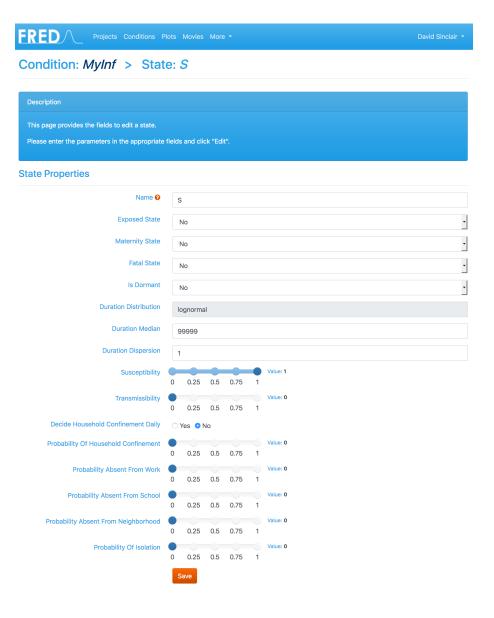


Figure 5: State creation

• Susceptibility: 0

• Transmissibility: 0

The exposed time and dispersion for influenza, along with other respiratory infections, are reviewed by Lesser *et al* [12]. Now the Infectious and symptomatic state can be added. We assume that infectious and symptomatic agents have a 50% chance of confining themselves to their households when ill, and they decide whether to do so for the length of their infectious and symptomatic period at the onset of symptoms (rather than potentially changing their mind each day). The mean infectious period and dispersion are from Ling et al [13].

• *Name:* Is

• Exposed State: No

• Duration Distribution: lognormal

• Duration Median: 5

• Duration Dispersion: 1.5

• Susceptibility: 0

• Transmissibility: 1

- Probability Of Household Confinement: 0.5
- Decide household confinement daily: No

However, it is possible to be infectious with influenza and be asymptomatic. We can create a separate State to account for the reduced transmissibility of influenza by asymptomatic agents and that asymptomatic agents would not elect to confine themselves to their household due to illness.

• Name: Ia

• Exposed State: No

• Duration Distribution: lognormal

• Duration Median: 5

• Duration Dispersion: 1.5

• Susceptibility: 0

• Transmissibility: 0.5

• Probability Of Household Confinement: 0

• Decide household confinement daily: No

Finally, we define the Recovered state, where they will be unsusceptible to further influenza. Asserting that Recovered is a dormant state will decrease the simulation's runtime.

• *Name:* R

• Exposed State: No

• Duration Distribution: lognormal

• Duration Median: 9999

• Duration Dispersion: 1

• Susceptibility: 0

• Transmissibility: 0

• Is Dormant: Yes

#### 4.3.2 Transitions between States

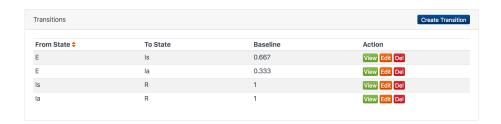


Figure 6: Transition probabilities

Now we have a list of States for the Condition MyInf, we must determine how agents transition between these States.

In FRED, transitions occur with a probability p once an agent has been in a State for the period defined by its distribution, median and dispersion. For example, we defined the E State with a duration median of 1.9 days and duration dispersion of 1.23 days. Therefore, FRED will attempt to transition an agent in the E State to another State after 1.9 days on average. We must define what State(s) the agent can transition to, and what the probability of it happening is.

Select the *Create Transition* button on the *MyInf* Condition page (n.b. the *Create Transition* button only becomes available once two-or-more States have been defined for a Condition).

We do not need to define a transition between the S and E States, as we have previously asserted that this happens automatically on exposure. Therefore, the first transition we define is from E to Is. This is simply a matter of selecting the E State in the From State on the drop down menu and Is in the To State drop down menu. We will assume that  $\frac{2}{3}$  of agents with influenza become symptomatic, with the other  $\frac{1}{3}$  becoming asymptomatic [6, 14], hence assign a baseline probability of transitioning to Is as 0.667. Please Save and repeat the process for E to Ia with baseline probability 0.333. All of our infectious agents will enter the R state (as we will not allow either death or perpetual infectiousness to occur), hence provide transition from both Is and Ia to R with probability 1. Your transitions should look similar to fig. 6.

You now have a model for simulating an influenza outbreak in FRED Web.

Full details on how FRED calculates probabilities of transitions for when probabilities do not sum to 1 are given in section 8. It is also explained here how to account for multiple transition factors which may each individually alter transition probabilities (for example, you may want to create a model in which the probability of an agent entering a State called 'cardiovascular\_disease' is both age and gender dependent).

It is important to note that if the transition probabilities from a State do not sum to 1, FRED will normalize the entered probabilities to a value of 1. Hence, if you wish to create a model where agents have a 75% chance of transitioning from State A to State B and a 25% chance of staying in the same State, you would need to define the transition State A to State A with p=0.25. as well as State A to State B with p=0.75.

# 4.4 Running a FRED Web job

### 4.4.1 Create Job

To run a simulation in FRED using your *MyInf* Condition, select the *Projects* tab in the top banner, click on the project you want the simulation to be associated with (i.e. *MyFirstProject*), and select *Create Job*. This will show the *Job Setup* page.

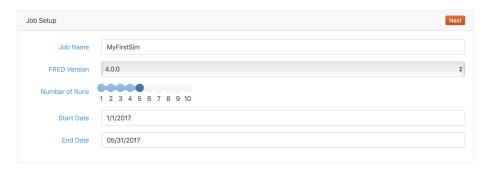


Figure 7: Job setup page

In the *Job Name* box provide a unique identifier for this simulation, which will allow you to access the simulation results afterwards. We will use MyFirstSim. You may select a version of FRED to use with the *FRED Version* menu, but it's advisable to use the latest version available unless you wish to compare this simulation to ones conducted on a previous version of FRED.

FRED use stochastic processes to seed and spread outbreaks. By running a simulation multiple times, a distribution of results will be generated, which can be used to determine standard errors and confidence intervals. More runs of the same simulation will give a more accurate distribution of your model's results, but at the cost of taking a longer time to run. We will select 5 runs from the *Number of Runs* slider.

The *Start/End Dates* allow the user to select the length of time of the simulation. Please note, dates are shown in month-day-year format. Schools and most workplaces in FRED are closed on weekends, so days of the week can influence simulation results. Leave the *Start Date* as is, and select May 31 2017 for the end date. Press *Next* 

### 4.4.2 Location Selection

The Location Selection options allow the user to specify which synthetic population to use. FRED Web currently supports any location in the 50 US states and the Indian state of Telangana. FRED Web allows users to select multiple County-level

areas if desired. The larger the population of the selected area(s), the longer a simulation will take to complete. We will use Jefferson County in Pennsylvania, a county of  $\sim 45\,000$ .

#### 4.4.3 Condition Selection

The *Condition Selection* options allow the user to specify which Conditions to use in the simulation. You will notice there are options in the Shared Conditions box, but we will select the Condition we have created, MyInf. Shared Conditions are pre-made Conditions available for users to include in their simulations if desired. Press *Next*.

#### 4.4.4 Visualize

You will now be presented with the *Visualize* options. Here users can select States to be tracked in detail and be available for display in a movie of the simulation. We will select MyInf.E. The more options selected, the longer the simulation will take to run. Press *Next*.

# 4.4.5 Imports

Now the *Imports* options will be displayed. Although you have created a model for simulating an influenza outbreak, there must be influenza present in the population to initiate an outbreak. In a real-world epidemic, this might occur when an exposed individual travels to a previously uninfected area. In FRED Web, this is imitated using the *Imports* options. Within *Imports*, all the Conditions selected for simulation will be selectable; we only have *MyInf* available. Now we can specify when, where, which and how many agents are randomly selected to be exposed to influenza to seed outbreaks, using the following options

- Start Day and End Day specify the range of simulation days in which to seed new influenza cases. Select 0 and 5.
- *Type of import* allows the user to specify the number of cases to import each day. If a number, n, is entered in Max, n agents will be automatically exposed per day between  $Start\ Day$  and  $End\ Day$  (provided there are n unexposed agents available). An alternative option is Fraction, which exposes the stated fraction of the susceptible population per day, rather than an absolute number. We will select Max and enter 3.
- Restrict by location allows the exposed agents to be limited to a specified area. This is controlled by entering the Latitude, Longitude and Radius. If No is selected, any agent within the population may be chosen. Radius has units of kilometers, Latitude and Longitude use decimal form. We will select No.
- Restrict by age allows an agent age range to be specified for the imported cases, with Min Age and Max Age. We will select No.

With these options selected, click *Add import*. This saves the selected imports and allows the user to enter further imports if desired. Press *Next*.

# 4.4.6 Additional Parameters

The *Additional parameters* options will be displayed. This text box can be used to include additional commands for the FRED job. We will not be using this feature for this job, so leave it empty. Press *Next*.

The *Review and submit* page will now be displayed, which should look similar to fig. 8. Here you can check your job options. When ready, click *Submit Job*, to submit your simulation to the FRED Web cluster. The job you have just submitted, *MyFirstSim* will be listed, alongside its current status. Initially the job status will be *submitted* - this means it is awaiting an available core on the FRED Web cluster. When one becomes available (hopefully this will not take long) the status will change to *executing*. When the job is finished, the status will be updated to *completed*. If you submitted a large job, this may take several hours, however this job should only take a maximum of a few minutes once it begins executing.

# Please review all of your settings for this simulation. Use the "Back" button to make any changes Review and Submi Variable Name Selection Job Name MyFirstSim FRED Version 4.0.0 Number of Runs Start Date 1/1/2017 End Date 4/1/2017 Country United States Locations PA-Jefferson Conditions A simple influenza model (MyInf) States to Visualize Imports Condition to Import Start Day **End Day** Fraction Latitude Longitude Radius Min Age Max Age

#### **Create Job**

Figure 8: Job summary page

## 4.5 Reviewing results

Within FRED Web there are three ways of reviewing results: looking at the CSV (comma separated values) file, creating movies and creating plots. First we will explain how to download the CSV file, and then how to create movies and plots.

When your job is *completed*, click on the job's name (MyFirstSim) to be taken to the *Results* page. Here you may download a CSV file containing the simulation results, should you wish to analyze them away from FRED Web. The CSV file contains the number of agents in each State of your model, for each iteration of your job. The CSV file also provides the number of new agents in each state each day, and the total number of agents to have ever been in each state, for each day of the simulation. Additionally, an 'RR' column will be produced for each condition. This is the 'Reproductive Rate' of each Condition. This is the mean number of agents each infective agent infects, for each day of the simulation. It is akin to the basic reproductive number,  $R_0$ , but for each time-step in the simulation.

# 4.5.1 Creating a FRED Web movie

To create a movie of your model, select *Projects* and access your project. Scrolling down will show the *FRED Movies* section. Select Create Movie. Use the drop down menu in *Step 1* to select the job for which you wish to create a movie (*MyFirstSim*) and click Find Variables to Display.

In *Step 2* provide a *Movie Name*, which FRED Web will use to save and load the movie (we will use MyFirstMovie). You may provide a *Title* and *Subtitle*, which will be displayed in the animation (we use Movie of Influenza and Jefferson County, PA for the *Title* and *Subtitle*, respectively). If provided, the *Left Caption*, *Center Caption* and *Right Caption* will be displayed underneath the animation with the selected colors. These can be used as a legend for the movie. We will enter Exposed agents into the *Left Caption* box, select *Red* for color, and leave the others blank.

Checking Show Census Tracts and Add grid will superimpose them on the movie (these options are not currently functional).

The movie will only show one iteration of the simulation. By default this is run 1, but it can be changed with the *Run number* option.

Line width adjusts the width of outlines in the plot (not currently functional). Min X, Max X, Min Y and Max Y allow the

movie to be focused on a particular geographic region using latitudes and longitudes (all of the counties selected will be displayed if no values are entered). *Start Day*, *End Day* and *Interval* allow the days of the simulation displayed in the animation to be limited and use different time-steps. We will leave all these options blank.

Step 3 lists the States available to be visualized. These are the States previously defined in the *Visualize* menu. Here, you will have the options of *MyInf.E* and *MyInf.newE*, where 'new' means new cases that time-step. Select the *Display?* checkbox for *MyInf.E*. You may also choose a point size and color for the markers in the movie, but these are fine to be left as their default values. Leave the *Period* option blank as this is not currently functional.

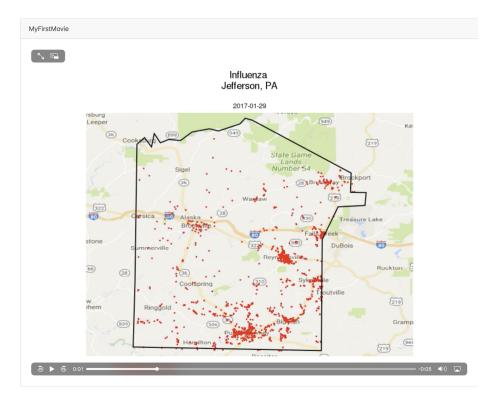


Figure 9: Movie of influenza in Jefferson County, PA

With your movie options entered, select Create the movie. Your Movies page will be displayed, showing the status of your movie, as well as any of your previously created movies. When *MyFirstMovie* is completed, click on its name to view the movie (the page should look similar to fig. 9). The movie shows dots superimposed on a map of Jefferson County. Each dot reveals the household location of every agent in the State *MyInf.E* at each time-step in the movie. Notice how initially only a small number of agents are in the *E* State; these are the imported cases. Very quickly, however, a large number of exposed agents appear in the County's population centers (such as Punxsutawney and Brookville if you are simulating Jefferson County, PA). A smaller number of exposed agents are shown in the low-population areas and very few, in any exposed agents are displayed in areas such as State Games Lands Number 54, where the population count is extremely low.

Users can access movies they have previously created opening the relevant project in the Projects menu and scrolling down to *FRED Movies*.

Movies can be downloaded by viewing the movie, and right-clicking on it.

## 4.5.2 Creating a FRED Web plot

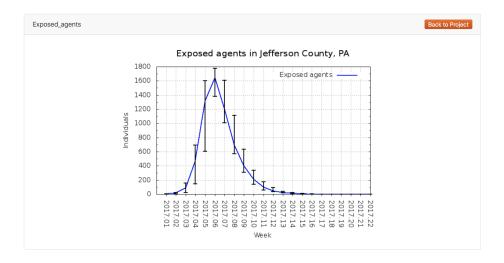


Figure 10: Plot of influenza prevalence in Jefferson County, PA

To plot simulation results, select *Projects*, select your project name and click *Create Plot* in the *FRED Plots* section. Choose the job to plot (*MyFirstSim*) and click Find Variables to Plot.

Provide a *Plot Name* for FRED Web to save the plot (we use Exposed\_Agents), as well as a title to be displayed on the plot (we use Exposed agents in Jefferson County, PA). Other options are available for displaying all runs or the mean results, a line chart or bar chart and displaying error bars (these display to stochasticity of the simulations, at 1 standard deviation). *By week* will plot weekly counts, rather than daily counts (check *By week* and *Error Bars*). The *Normalize* checkbox can be checked to display results per 100,000 people, instead of raw counts. If *Normalize* is checked and a value is entered into the *Denominator* box, the plot can be normalized by arbitrary values. *Min X, Max X, Min Y* and *Max Y* allow axis limits to be asserted.

Step 3 will be displayed below, listing variables from your job which can be displayed. We will plot the number of exposed agents as a function of time. Select the check box for *Job: MyFirstSim Plot Variable: MyInf.E*, change the label to Exposed agents and select the color Green from the drop down menu.

With your options selected, click Create the Plot to view the plot (which should look similar to fig. 10). The error bars are relatively large, owing to the small number of runs and relatively small population simulated.

Go back and now create a plot with *MyInf.E*, *MyInf.Is* and *MyInf.Ia*, making sure to select different colors for each State. Uncheck *Error Bars* and *By Week* and click Create the Plot. You will notice approximately twice as many *Is* agents as *Ia* agents, and that the curve of the *E* agents leads the infectious curves. You may also notice small peaks and troughs in the curves. These are occur at approximately 7 day intervals and highlight the smaller number of exposures that occur at weekends compared to week days (as fewer agents are mixing in schools and workplaces).

To plot the Attack Rate, select *MyInf.totE* and *Normalize* the plot, with a denominator of 100.

Users can access plots they have previously created opening the relevant project in the Projects menu and scrolling down to *FRED Plots*.

Plots can be saved by right-clicking and selecting Save image as....

# 5 Social distancing

Now you have the template for running and analyzing FRED Web jobs. In the next example we will incorporate simplified human behavior into the model. The model will again simulate an influenza outbreak, with the added element of perceived risk allowing agents to engage in social distancing. Studies suggests that some Americans increased their household confinement during the 2009 H1N1 pandemic; this behavior change may have decreased the influenza outbreak's attack rate [15]. To simulate this behavior, we will create a Condition which allows agents to reduce their neighborhood interactions if the fraction of agents symptomatic with flu in their neighborhood exceeds a critical threshold.

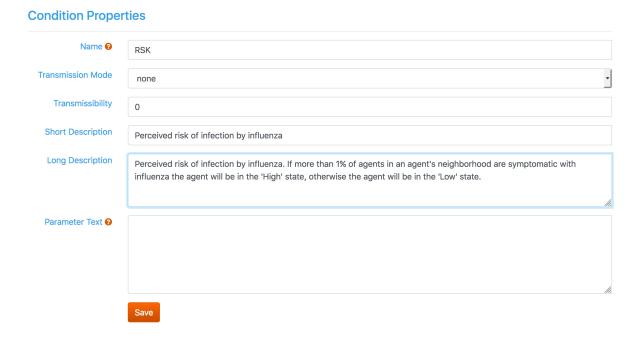
In a default FRED model, each agent visits their household, workplace/school and neighborhood each day<sup>2</sup>. Neighborhoods

<sup>&</sup>lt;sup>2</sup>Agents who are unemployed do not interact with other agents at a workplace or school. Most agents work Monday-Friday, although a minority work

are defined as a 1 km<sup>2</sup> area around an agent's household. We can control agents' daily behavior by specifying their probability of being absent from their workplace, school or neighborhood, confining themselves to their household or isolating themselves from every other agent, for each State they could occupy. These options are found on the *State Properties* page.

#### 5.1 RSK Condition

We will create a new Condition, called *RSK*, which sets each agent's perceived risk of infection. To create the new Condition, select Conditions in the top banner and select Create Condition. Give the Condition the name *RSK*. We do not want this to be a transmissible condition, so set *None* for the Transmission Mode and leave Transmissibility as 0. We will be using the Parameter Text to control some of State transition behavior in this model, but we will first construct the basic *RSK* Condition using the point-and-click interface. Add a short and long description, explaining that this Condition will set each agent's perceived risk to infection (you can copy the description in fig. 11). Click Save.



**Figure 11:** Create the *RSK* condition, which sets each agent's perceived risk of infection.

We now want to create the two States of the *RSK* Condition: *Low* and *High*. As before, create the States using the Create State button. As *RSK* is not a transmissible Condition, we can leave most of the *State Properties* options as their default settings. We need only specify two things: first, how frequently agents evaluate whether to switch between the *Low* and *High* states; and second, that agents in the *High* State of *RSK* will be more likely to avoid interacting with their neighbors than those in the *Low* State. Use the Duration Median option to specify how long an agent stays in the *Low* and *High* States before evaluating whether they should make a transition to another State: we will use 7 days. In the State Properties of the *High* State, set the Probability Absent From Neighborhood slider to be non-zero: we will use 1, which means any agent in the *High* State of Condition *RSK* is guaranteed to avoid interacting with other agents in their neighborhood. This is probably an exaggeration of most real behavior, but allows the effect of agents avoiding neighborhood interactions due to their high perceived risk of infection to be more pronounced in our model. An image of the *High* State's properties are given for reference in fig. 12.

weekends. Neighborhood interactions increase 50% on weekends by default

#### **State Properties**

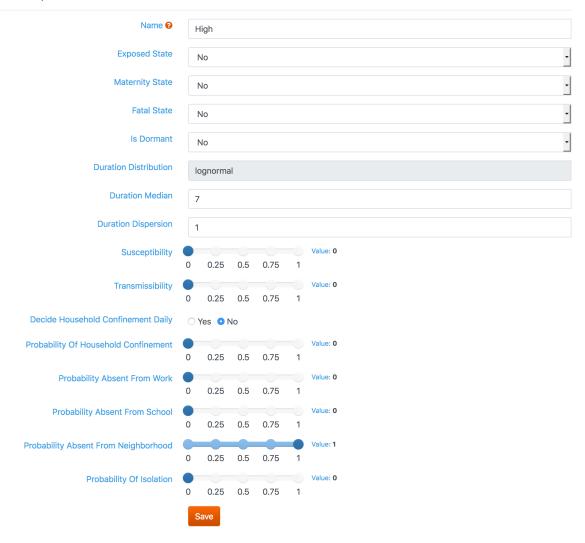


Figure 12: Create the RSK condition, which sets each agent's perceived risk of infection.

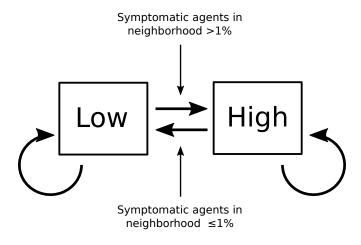


Figure 13: State diagram for the RSK condition, which sets each agent's perceived risk of infection.

Now we need to define the transitions between the *Low* and *High* States: what will determine whether an agent perceives themselves as at low or high risk of being infected? For this demonstration we will use a simple model. We will assume that agents consider themselves at low risk, unless the prevalence of symptomatic agents in their neighborhood exceeds a critical threshold, at which point they consider themselves at high risk. If the prevalence drops below this critical threshold, an agent will revert back to considering themselves at low risk. This is illustrated in fig. 13.

To construct State transitions which correspond to this behavior we need to use both the transition probabilities options on the Condition: RSK page and the Parameter Text box in RSK's Condition Property page. We will start with the simple transitions that can be set with the state transition options you have used previously. The transitions specified here give the baseline transitions in the model, which will apply unless transitions specified in the Parameter Text text box overrule them. As we want agents to remain in the Low State by default (or return to the Low State from the High State by default), specify the transitions to do this. This can be achieved using the following transitions for the States:

• Low  $\rightarrow$  Low: 1

• Low  $\rightarrow$  High: 0

• High  $\rightarrow$  High: 0

• High  $\rightarrow$  Low: 1

# 5.2 Including condition-level transition factors

Now we can add additional transition options using the Parameter Text box. Access the Parameter Text box by clicking on Edit in the top-right of the Condition: *RSK* page (as shown in fig. 14). You will see that the Parameter Text text box has been filled with text. Reading the text, you will recognize it as a text version of the *RSK* Condition you have created, defining the *Low* and *High* States, with their durations and transitions. You will also see that the probability of being absent from the neighborhood is specified. At the bottom of the text box you will also see some commented out metadata, which contains the Condition name and description.

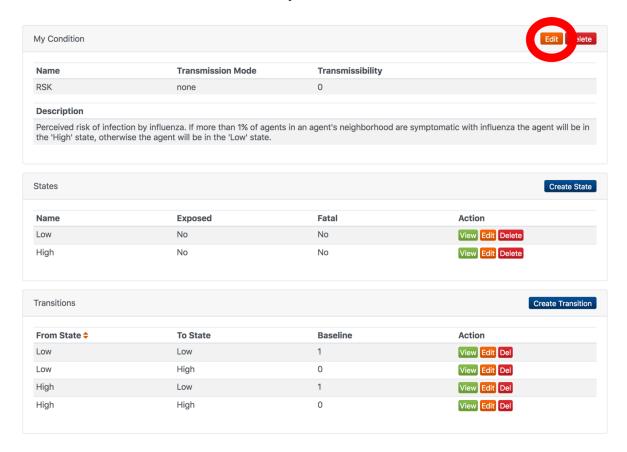


Figure 14: Edit the condition, to access the Parameter Text text box.

We can use the Parameter Text text box to add more complex transitions and model components. We will call these transition factors. Find the line in the Parameter Text which specifies the chance of an agent transitioning from the Low to the High RSK State. It should read

RSK.transition[Low][High] = 0

Breaking this into its component parts,  $\underline{RSK}$  is the Condition name,  $\underline{transition[Low][High]}$  specifies the transition from State Low to State High and  $\underline{=0}$  specifies that the probability of this  $\underline{transition}$  is zero. This is the default probability of

transitioning from *Low* to *High*, but we can specify scenarios in which this probability can be altered. For example, if we wanted there to be a 20% chance that agents over the age of 60 will transition from the *Low* to the *High* State, we could add, on a new line in the Parameter Text, the following:

```
RSK.transition[Low][High].age_is_60+=0.2
```

RSK.transition[Low][Low].age\_is\_60+ = 0.8

Do not simply append  $\underline{.age\_is\_60+=0.2}$  to the existing  $\underline{RSK.transition[Low][High]}$ , as FRED requires the default transition to be specified.

Adding the line with RSK.transition[Low][High].age\_is\_60+ = 0.2 means that agents who are specified in the synthetic population as aged 60 or above will transition from the Low State to the High State each time the transition is evaluated (which we specified to be every 7 days), with a 20% probability (and have an 80% chance of remaining in the Low State). It is important to specify the  $Low \rightarrow Low$  transition probability as well as the  $Low \rightarrow High$  transition probability, as otherwise FRED will normalize the  $Low \rightarrow High$  transition probability, for agents over the age of 60, to be 1. Additionally we could specify

```
RSK.transition[Low][High].currently_in_state_MyInf.R = 0.3
```

RSK.transition[Low][High].currently\_in\_state\_MyInf.R = 0.7

<u>currently\_in\_state\_MyInf.R</u> means that any agent who is currently in the *R* State of the MyInf Condition will make this transition with 30% probability (n.b. this only works if the MyInf Condition is included in the FRED Job along with the RSK Condition, but of course you can substitute alternative Conditions and States!)

Be careful using probabilities if multiple transitions which apply to the same agent are specified (for example, if both of the above transition factors were specified and there was an agent over the age of 60 in the *MyInf.R* State) as the transition probabilities may act in an unexpected way. Transition probabilities using multiple transition factors can be evaluated using a logistic model in FRED, but this feature is not yet included in the FRED Web interface. The user can, however, calculate their own logistic regression and input the resulting probabilities to FRED Web. This is explained further in section 8.

For our model, we want agents to enter the *High* State of *RSK* if a critical threshold of their neighbors exhibit symptoms of influenza. We can do this with the following commands in the Parameter Text text box, as shown in fig. 15.

```
RSK.transition[Low][High].fraction_in_Neighborhood_excluding_agent_exceeds_level_1_in_state_MyInf.Is = 1
```

RSK.transition[Low][Low].fraction\_in\_Neighborhood\_excluding\_agent\_exceeds\_level\_1\_in\_state\_MyInf.Is = 0

RSK.transition[High][High].fraction\_in\_Neighborhood\_excluding\_agent\_exceeds\_level\_1\_in\_state\_MyInf.Is = 1

RSK.transition[High][Low].fraction\_in\_Neighborhood\_excluding\_agent\_exceeds\_level\_1\_in\_state\_MyInf.Is = 0

With apologies for the length of the command strings, we can break the command down to understand what it is doing (these command strings are case-sensitive, so please remember to capitalize Neighborhood). As before <u>RSK</u> specifies the Condition and transition[Low][High] specifies the transition. For each agent, fraction\_in\_Neighborhood\_excluding\_agent indicates the fraction of other agents in their neighborhood, <u>exceeds\_level\_1</u> specifies the critical threshold that the fraction must be over to trigger this transition command, <u>in\_state\_MyInf.Is</u> specifies the Condition and State to be used to calculate the fraction of neighborhood agents occupying a <u>State</u>.

#### **Condition Properties**

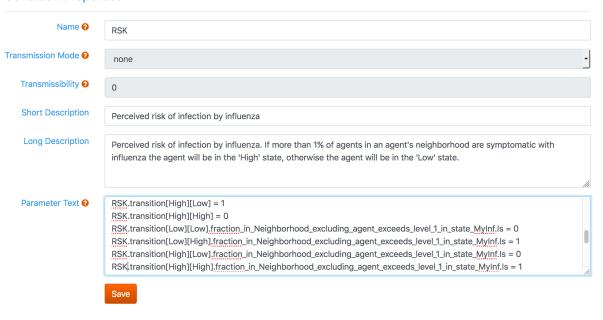


Figure 15: Entering transition factors in the Parameter Text box.

Level\_1 corresponds to 10% by default, so if  $\geq 10\%$  of the other agents in a neighborhood are symptomatic with flu (i.e. in State MyInf.Is) then an agent will move from State RSK.Low to State RSK.High with a probability of 1. The value of level\_1 cannot currently be adjusted in FRED Web. However, different thresholds can selected using level\_1 to level\_5. These correspond to 10, 20, 30, 40 and 50%, respectively.

Once you have created the RSK condition, you can create and run a job using it. As previously, select your Project, click  $Create\ Job$  and select your job options. On the  $Condition\ selection$  screen, include both MyInf and RSK. Select both MyInf. E and E and E and E imports your influenza condition, and not the E condition, otherwise there will be no agents with influenza to seed the outbreak). It is not necessary to import any cases for E imports your influenza to seed the outbreak.

When the job has finished running, create some plots and movies. Does the number of agents in the RSK.High State seem consistent with the number of agents in the MyInf.Is State?<sup>3</sup> Compare the attack rate of influenza in this simulation to the one you previously ran in which agents did not take any social distancing measures (attack rate is the total number of cases in the susceptible population divided by the total susceptible population, it can be plotted using the Normalize check box, entering a Denominator of 100 and plotting the total number of exposed agents). Compare how the prevalence of influenza at different days is altered between the simulations. Try running further jobs in which the critical threshold for agents to take social distancing measures,  $Neighborhood\_fraction\_level\_1 = f$ , is set to other values.

# 6 Vaccination

Vaccination acceptance presents an alternative behavioral change option. We can include a further Condition which describes vaccination, in which agents who perceive themselves as being high risk for influenza infection (i.e. in the *RSK.High* state) are more likely to seek a vaccine. A simple implementation of this is given in fig. 16.

 $<sup>^3</sup>$ If things don't look as expected, you can compare your Condition to the *RSKw* Shared Condition (Conditions  $\rightarrow$  Shared Conditions  $\rightarrow$  RSKw) to see if there are any discrepancies.

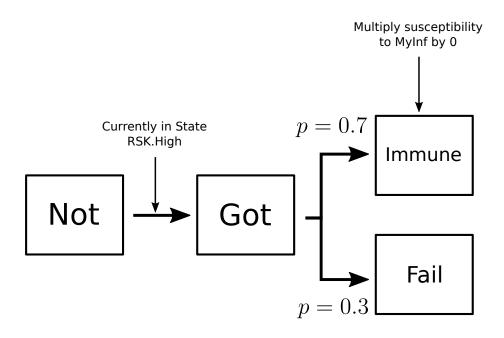


Figure 16: State diagram for a simple vaccine model

This Condition can be created using the same approach as the previous Conditions. To aid implementation, some suggestions are offered. In this Condition (which we call MyVac), all agents start in the Not State, indicating they are not intending to seek a vaccine. Agents should evaluate whether to remain in this State or transition to the Got State every day (so set the duration of the Not State to be 1 day), but only transition agents to the Got state if they perceive themselves as at high risk of infection (i.e. they are in the RSK.High State). The following transition factor can be used in the Parameter Text text box.

MyVac.transition[Not][Got].currently\_in\_state\_RSK.High = 1.0

MyVac.transition[Not][Not].currently\_in\_state\_RSK.High = 0.0

Vaccines are not successful for everyone. We can assume the 70% of agents who receive a vaccine become immune, while 30% do not. It can take  $\sim 14$  days for a vaccine to become fully effective, so include this duration period before transitioning agents from the *Got* to the *Immune / Fail* States. Agents in the *MyVac.Immune* State can be prevented from entering the exposed state of the MyInf Condition (MyInf.E) by altering each agent in the MyVac.Immune State's susceptibility to the MyInf Condition. This can be done with the following Condition Parameter Text.

MyVac.Immune.multiply\_susceptibility\_to\_MyInf = 0

The Shared Condition: VACw is available to compare your model against, if desired <sup>4</sup>. The impact of the vaccination behavior is dependent on how early in the influenza outbreak agents start receiving vaccinations, and the time it takes for vaccinations to become effective. These parameters can be adjusted to investigate this.

# 7 Additional exercises

You now have the knowledge to create a wide-range of models in FRED Web. If you wish to create your own FRED models, you can consult a full list of transition factors currently supported by FRED in section 9. Alternatively, you could consider the following exercises

- Define a new influenza model that has 80% of the transmissibility of the baseline influenza model, but with a symptomatic infectious period with median 10 days and dispersion = 2.0. How do these variations affect the timing and amplitude of the epidemic peak? What is the projected attack rate
- Change the *Probability of Household Confinement* with *influenza\_symptomatic* and *influenza\_asymptomatic* to 80%. Then, to 0%. How does the attack rate change? How is the duration of the epidemic affected?
- Alter the immunization Condition so that a percentage of agents start off immune to influenza, using pre-emptive vaccination levels of 10%, 20%, 30%, 40% and 50%. How does this change the outbreak? What are the projected attack rates for each level? How much immunization is needed to result in an attach rate below 10% of the population.

 $<sup>^4</sup>Accessed$  by Conditions o Shared Conditions o VACw

• Design your own model. Use the full list of transition factors in section 9.

# 8 Transition probabilties

## 8.1 Probabilities

Transition probabilities can most easily be set in FRED Web using the Create Transition options on the Condition page. Here a numerical value between 0 and 1 is given.

In FRED parameter text, a transition probability between State A and State B, of the Condition COND, is given by

COND.transition
$$[A][B] = p$$

where p is the transition probability.

If no transition probabilities are provided, FRED defaults to transitioning to the same State an agent is already in. This can be altered in parameter text with the command

$$COND.A.default\_next\_state = x$$

where x is the new State to transition to by default.

If the sum of the transition probabilities out of a State is greater than 1, FRED will normalize all the transition probabilities by dividing each of the transition probabilities by the sum of the transition probabilities. For example, if the user specifies the following probabilities for transitions from State A to States A, B and C:

COND.transition[A][A] = 0.7

COND.transition[A][B] = 0.3

COND.transition[A][C] = 0.2

FRED will normalize the user-provided probabilities to give the following normalized probabilities:

$$A \rightarrow A = 0.7/(0.7 + 0.3 + 0.2) = 0.583$$

$$A \rightarrow B = 0.3/(0.7 + 0.3 + 0.2) = 0.250$$

$$A \rightarrow C = 0.2/(0.7 + 0.3 + 0.2) = 0.167$$

On the other hand, if the sum of the transition probabilities out of a State is less than 1, FRED will simply increase the probability of the transition to the default next State, such that the sum of the probabilities out of the State equals 1. For example, if the user specifies the following probabilities for transitions from State A to States A, B and C:

COND.transition[A][A] = 0.1,

COND.transition[A][B] = 0.2,

COND.transition[A][C] = 0.3,

and does not alter the default next state (so it is set to be A), FRED will adjust the probabilities to give the following probabilities of each transition.

$$A \to A = 0.5 \,,$$

$$A \rightarrow B = 0.2$$
,

$$A \rightarrow C = 0.3$$
.

.

# 8.2 Logistic regression

Logistic regression can be used in FRED when multiple transition factors can influence the probability of which transition occurs. This is currently only supported through FRED's parameter text. This text is not the place for a full explanation of logistic regression, only the details necessary to implement its results in FRED are included.

Consider that the log-odds, l, of an outcome for a model with two variables can be described by

$$l = \beta_0 + \beta_1 X_1 + \beta_2 X_2 ,$$

where

$$l = \ln\left(\frac{p}{p+1}\right) \,,$$

in which p is the probability of an outcome occurring,  $\beta_i$  are coefficients and  $X_i$  are predictors (which are equivalent to transition factors in FRED).

The coefficient  $\beta_0$ , which corresponds to the default transition probability if no predictors are applicable, can be provided in FRED using

COND.transition[A][B].intercept = 
$$\beta_0$$
.

The inclusion of .intercept indicates to FRED that you are using logistic regression to determine transition probabilities. Declaring a transition with '.intercept' will overwrite any transitions set with probabilities. For example, if both of the following are declared

COND.transition[A][A] = 0.1,

COND.transition[A][A].intercept = 0.9,

then only COND.transition[A][A].intercept = 0.9 will be used by FRED.

If predictor  $X_1$  is that the agent's gender is male, then the coefficient  $\beta_1$  for predictor  $X_1$  can be included using

COND.transition[A][B].sex\_is\_male.coeff = 
$$\beta_1$$
.

The suffix '.coeff' is used when specifying the values of  $\beta_1, \beta_2, ..., \beta_n$ . Any transition factor that FRED supports (see section 9) can be used instead of sex\_is\_male. Further predictors can be included by simply adding additional lines to the parameter text, such as

COND.transition[A][B].age\_is\_60+.coeff = 
$$\beta_2$$
.

If  $\beta_0$ ,  $\beta_1$  and  $\beta_2$  have values of 0.1, 0.3 and -0.2, respectively, then an agent who is male and age 72, will have a log-odds of:

$$l = \beta_0 + \beta_1 X_1 + \beta_2 X_2,$$
  

$$l = 0.1 + (0.3 * 1) + (-0.2 * 1),$$
  

$$l = 0.2.$$

for making the transition  $A \to B$ . This corresponds to a probability of

$$p = \frac{1}{1 + e^{-l}},$$
  
 $p = 0.55,$ 

(the normalization processes described in section 8.1 will still be applied, however). Alternatively, for a female agent aged 81, the calculation would be:

$$\begin{split} l &= \beta_0 + \beta_1 X_1 + \beta_2 X_2 \,, \\ l &= 0.1 + (0.3*0) + (-0.2*1) \,, \\ l &= -0.1 \quad \text{therefore} \quad p = 0.48 \,. \end{split}$$

Most transition factors used in FRED yield a binary value (1 or 0), which means that when they are used as predictors,  $X_1, X_2, ..., X_n$ , they are a binary value. However, it is worth noting that a some of transition factors yield a non-binary value. These can generally be inferred from the transition factor name. Examples include sim\_day, age and log\_of\_age.

# 9 Transition factors

# 9.1 Brief explanation for the syntax for the transition factors in FRED

The following have categorical levels determined by the synthetic population data:

- descriptionhousehold\_size
- neighborhood\_size
- school\_size
- workplace\_size
- hospital\_size
- household\_income
- neighborhood\_income
- school\_income
- workplace\_income
- hospital\_income
- household\_elevation
- neighborhood\_elevation
- school\_elevation
- workplace\_elevation
- hospital\_elevation

For each of these, risk factors can specify

- quintile level (5 levels defined by the data)
- quartile level (4 levels defined by the data)
- min, low, medium, high, or max

By default, the categories min, low, medium, high, max are the same as the quintile categories. The defaults can be overridden by optional parameters of the form:

- PLACE\_X\_upper\_bound\_min = REAL\_VALUE
- PLACE\_X\_upper\_bound\_low = REAL\_VALUE
- PLACE\_X\_upper\_bound\_medium = REAL\_VALUE
- PLACE\_X\_upper\_bound\_high = REAL\_VALUE

where PLACE is any of {Household, Neighborhood, School, Workplace, Hospital} and X is any of {size, income, elevation}.

Example: suppose you want to have a transition from state A to state B in condition COND if the student attends a large school.

You could declare a transition probability like this:

```
COND.transition[A][B].school_size_is_in_fifth_quintile = 1.0
```

This would apply if the school size is in the top 20% of the schools in the simulation.

If you want to be more specific you could define the cutoffs for school size categories with parameters like:

 $School\_size\_upper\_bound\_min = 20$ 

```
School_size_upper_bound_low = 100
School_size_upper_bound_medium = 500
School_size_upper_bound_high = 1000
```

With these values, any school with more than 1000 students is assigned to the "max" category. So your transition could be defined as follows:

```
COND.transition[A][B].School\_size\_is\_max = 1.0
```

This would apply if the school size is over 1000 students.

NOTE: if the agent does not attend a school, then the transition factor does not apply.

For Household\_size and number\_of\_children, transition factors are defined for individual or minimum values for sizes up to 10, for example:

```
Household_size_is_2

Household_size_is_4+

number_of_children_is_2

number_of_children_is_0+
```

The plus sign means "greater or equal to given value".

#### 9.2 List of transition factors

Below contains an approximate list of all the transition factors currently available in FRED Web. Some of these factors will be self-evident, but some will not (and may require some investigation to figure out what they do if you're not the person who happened to add that transition factor to the source code!) These transition factors are primarily included here to give an idea of the flexibility in modeling that FRED currently supports. Additional transition factors are added to FRED all the time, and if there is something you would like to model that doesn't appear to have a relevant transition factor already, please feel free to contact the FRED team (using the Contact Us link under the Help banner of the FRED website) and we can see if we can help you and add the functionality.

#### 9.2.1 Time and Date

```
NOTE: N may be replaced by any non-negative integer.
```

NOTE: "MON" is a three letter month abbreviation, such as Jan, Feb, etc

```
sim_day_is_N
year_is_YYYY
date_range_is_MON-DD_to_MON-DD
date_is_MON-DD
```

## 9.2.2 The Agent's Demographics

```
NOTE: N may be replaced by any non-negative integer NOTE: Number of children C has range 0..10
```

```
age_is_N
age_is_N+
age_is_N-N
race_is_african_american
race_is_alaska_native
```

```
race_is_american_indian
race_is_asian
race_is_hawaiian_native
race_is_multiple
race_is_multiple
race_is_other
race_is_tribal
race_is_tribal
race_is_white
sex_is_female
sex_is_male
number_of_children_is_C 5
number_of_children_is_C+
```

# 9.2.3 The Agent's Activity Profile

```
is_employed
is_resident_in_college_dorm
is_resident_in_group_quarters
is_resident_in_military_barracks
is_resident_in_nursing_home
is_resident_in_prison
is_retired
is_student
is_teacher
is_unemployed
```

# 9.2.4 The Agent's Places

NOTE: PLACE can be Household, Neighborhood, School, Classroom, Workplace, Office, Hospital or any user-defined place type, as well as the pseudo-place-types AdminPlace or HostedPlace. AdminPlace refers to the place administered by the agent, if any. HostedPlace refers to the place hosted by the agent, if any.

NOTE: FIPS<n> is a US FIPS code with n digits.

NOTE: X may be replaced by any real number.

NOTE: Place mark M may be replaced by any integer from 1..8

NOTE: ADI is the Adjusted Disadvantage Index. ADI rankings R range from 1..10, with 1 indicating the least disadvantaged and 10 indicating the most disadvantaged.

```
is_admin_of_a_PLACE
is_host_of_a_PLACE
is_member_of_a_PLACE
block_group_admin_code_of_PLACE_is_FIPS12
census_tract_admin_code_of_PLACE_is_FIPS11
```

<sup>5&#</sup>x27;children' are defined by new agents created by a maternity state, not the number of children living in the same household

```
county_admin_code_of_PLACE_is_FIPS5

[elevation | income | size]_of_PLACE_is_in_[first | second | third | fourth]_quartile

[elevation | income | size]_of_PLACE_is_in_[first | second | third | fourth | fifth]_quintile

[elevation | income | size]_of_PLACE_is_[greater_thanlless_thanlequal_to]_X

PLACE_has_mark_M

adi_national_rank_of_PLACE_is_R

adi_national_rank_of_PLACE_is_R+

adi_state_rank_of_PLACE_is_R

adi_state_rank_of_PLACE_is_R+
```

# 9.2.5 The Agent's Own Conditions and Variables

NOTE: When COND or COND.STATE appear within a factor, they may refer to any condition or state defined by the model. NOTE: X may be replaced by any real number.

```
is_in_state_COND.STATE

was_ever_in_state_COND.STATE

is_susceptible_to_COND

is_transmissible_for_COND

was_ever_exposed_to_COND

was_exposed_to_COND_in_PLACE

my_COND.VAR_is_[greater_than | less_than | equal_to]_X

COND.STATE.change_state_from.CONDx.StateX_to = StateY [ StateX and StateY are in CONDx ]
```

## 9.2.6 Other Agent's Conditions and Variables

NOTE: X may be replaced by any real number

```
[incidence \mid current \mid total] = [count \mid percent] = of_COND.STATE = [in_PLACE = excluding_me] = is_[greater_than \mid less_than \mid equal_to]_X \\ sum_of_COND.VAR_in_PLACE_is_[greater_than \mid less_than \mid equal_to]_X \\ ave_of_COND.VAR_in_PLACE_is_[greater_than \mid less_than \mid equal_to]_X \\
```

#### 9.2.7 Numeric Factors

### **Date and Time**

sim\_day

## Random numbers

get\_random
get\_normal
get\_exponential

## The Agent's Demographics

```
age
age_squared
log_of_age
```

### The Agent's Own Conditions and Variables

```
my_COND.VAR
```

## Other Agent's Conditions and Variables

```
[log_of][incidence | current | total]_[count | percent]_of_COND.STATE[_in_PLACE][_excluding_me] sum_of_COND.VAR_in_PLACE ave_of_COND.VAR_in_PLACE
```

# References

- [1] Joshua M. Epstein, Jon Parker, Derek Cummings, and Ross A. Hammond. Coupled contagion dynamics of fear and disease: Mathematical and computational explorations. <u>PLOS ONE</u>, 3(12):1–11, 12 2008.
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