University of Pittsburgh

The New FRED
(the FRamework for Epidemiological Dynamics)

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PHDL Seminar

7 Aug 2017

Outline

- Overview of Modeling in FRED
- User-defined Conditions and States
- Duration of States
  - distributions
  - absorbing, dormant and transient states
- State Transitions
  - logic-driven
  - probabilistic
  - event-driven
- Examples
- Future tutorial topics
  - web interface
  - plotting and visualization

What is FRED?

- **FRED** is a **FR**amework for **E**pidemiological **D**ynamics
- **Framework:** FRED is not a model. FRED is a tool for building epidemiological models
- **Epidemiology:** the study and analysis of the patterns, causes, and effects of health and disease conditions in defined populations (Wikipedia)
  - Infectious and noninfectious diseases
  - Health-related conditions such as obesity, drug use, violence, vaccine acceptance, etc
- **Dynamics:** FRED is designed to study how patterns of health conditions in defined populations *vary over time*

FRED is designed to build agent-based (individual-based) models

Agent-based Models

- Include each person in the model, along with social contacts and interactions with the environment
- Include individual responses and behaviors in the model
- Investigate interactions between public health dynamics and spatially distributed resources such as health care facilities

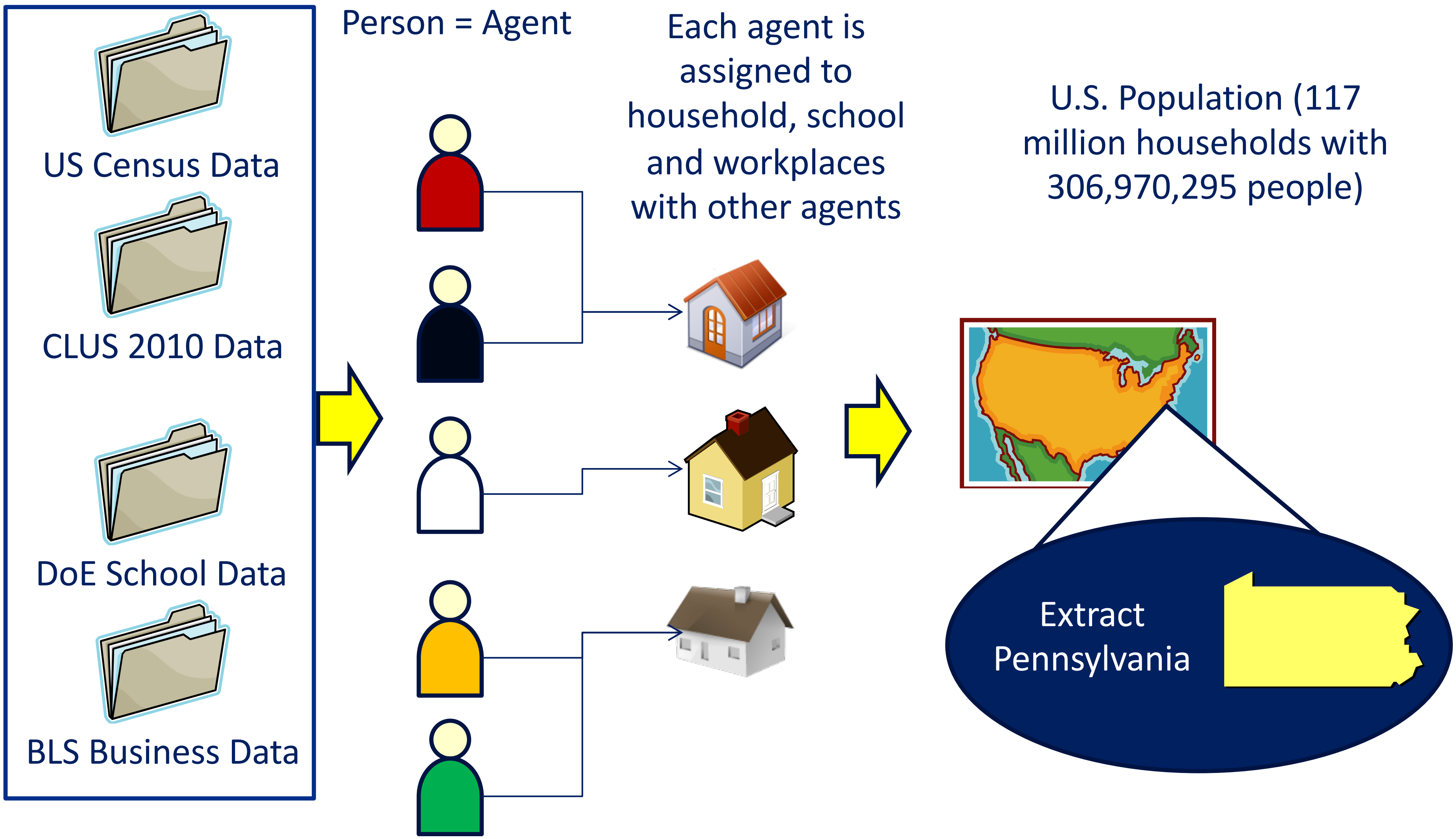
Purposes

- Study how interactions among *individuals and their environment* can result in patterns of *population behavior*
- Study the *impact of policy and programs* on public health

Foundational Concepts in FRED

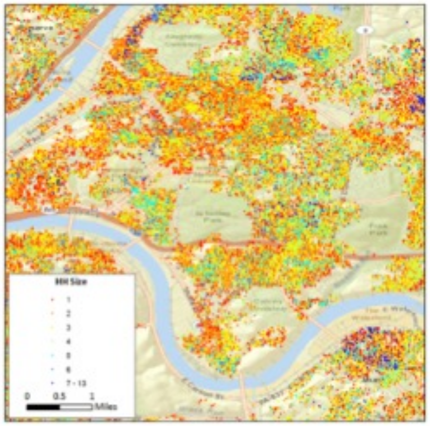
- Space
  - Two-dimensional geography based on actual locations
  - Future: 3-dimensional landscape (e.g. altitude)
- Time
  - Time step = 1 day (agents have multiple serial activities per day)
  - Duration = 1 day to 100 years
- Agent = individual person
- Places (mixing groups for agents)
  - Households, neighborhoods, workplaces, schools, hospitals
  - Future: other place types
- Population
  - Based on census data and other sources
  - Agents are associated with specific places

Census-matched Synthetic Population

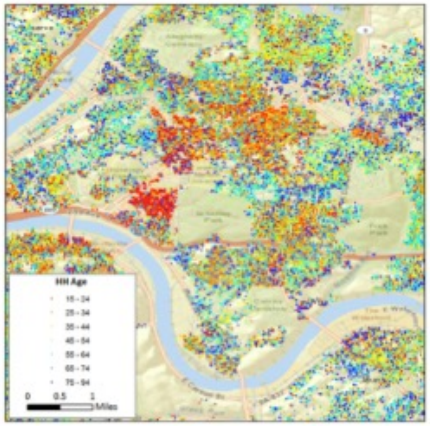


Matches Actual Demographics

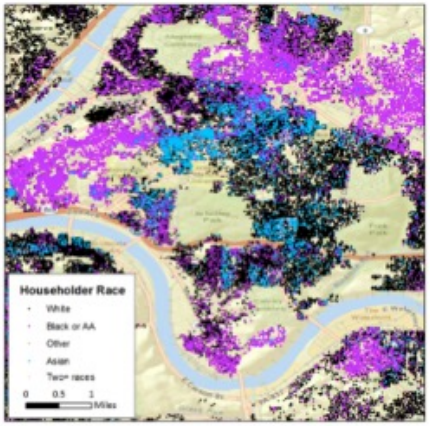
- Iterative proportional fitting assures that synthetic attributes are distributed as real ones are



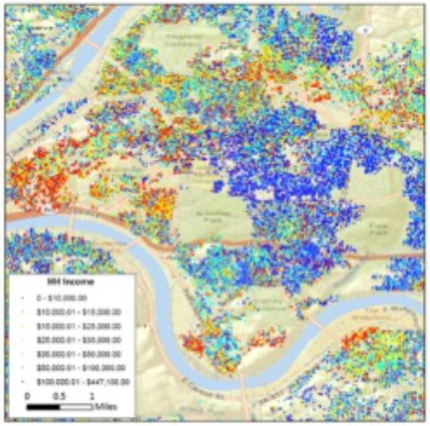
Household Size



Age



Race



Income

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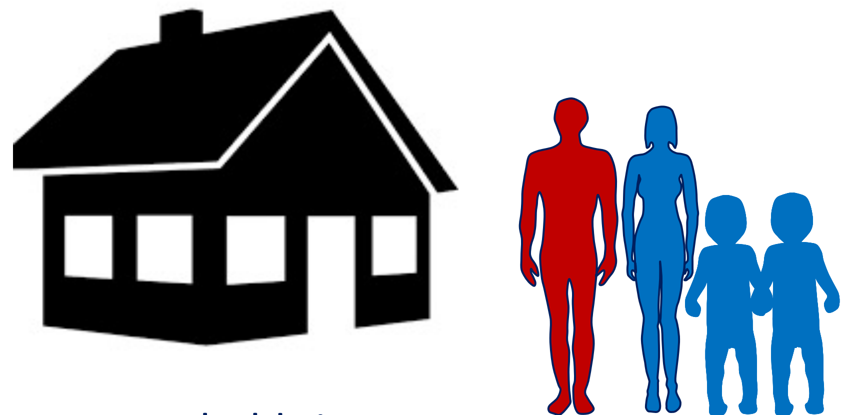
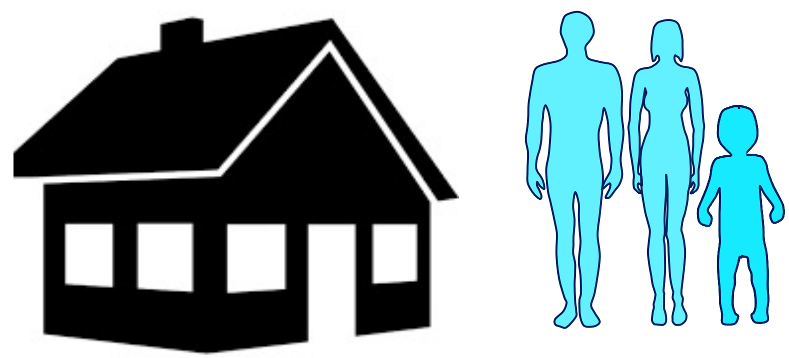
FRED Daily Dynamics

Location and size of each school

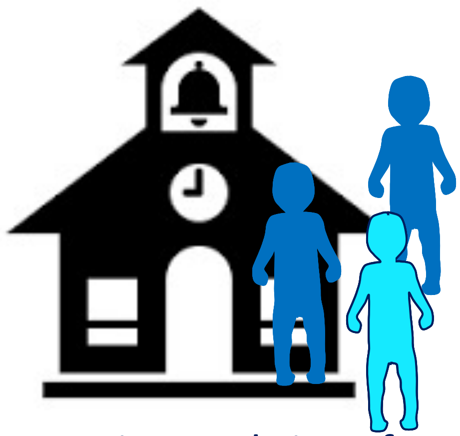


Household size, ethnicity, ages, income

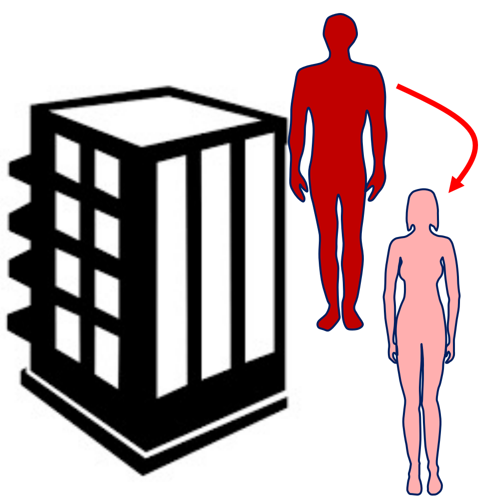
Location and size of each workplace



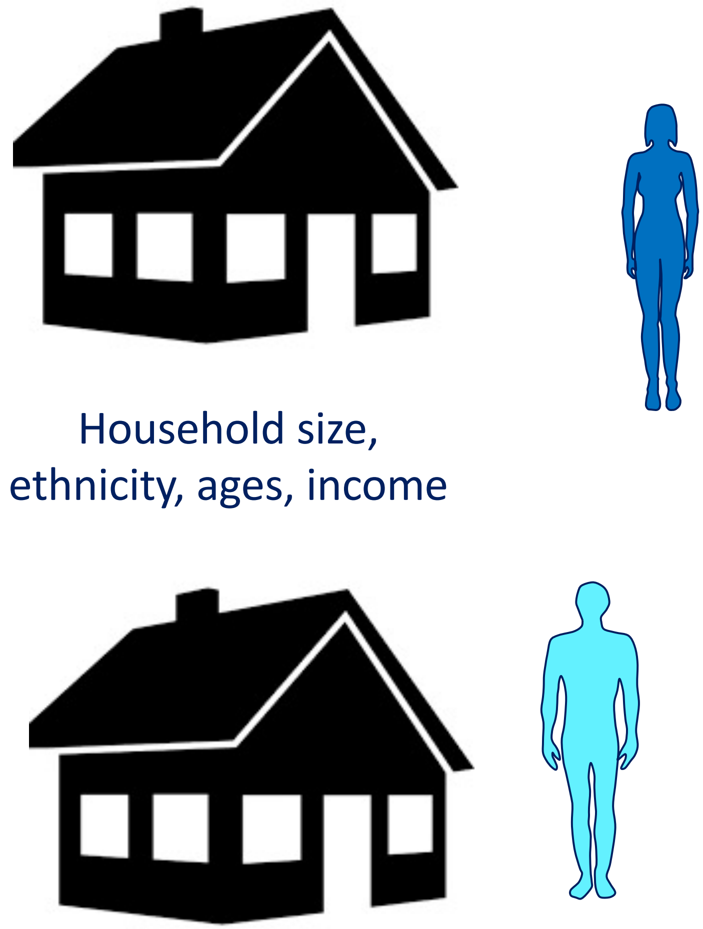
FRED Daily Dynamics



Location and size of each school



Location and size of each workplace



Household size, ethnicity, ages, income

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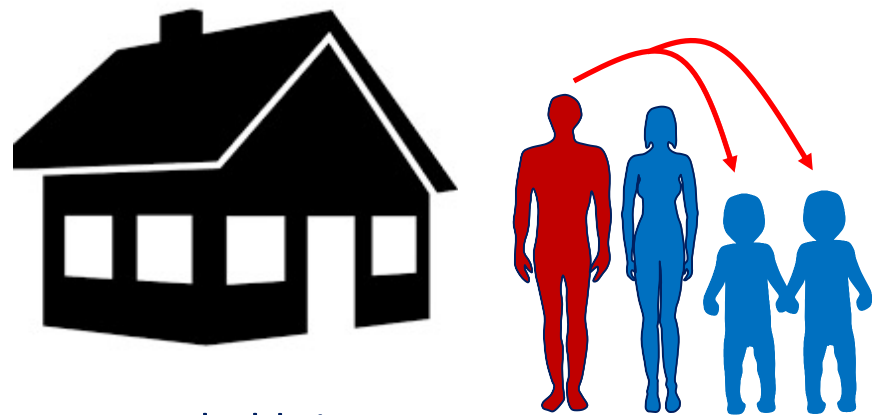
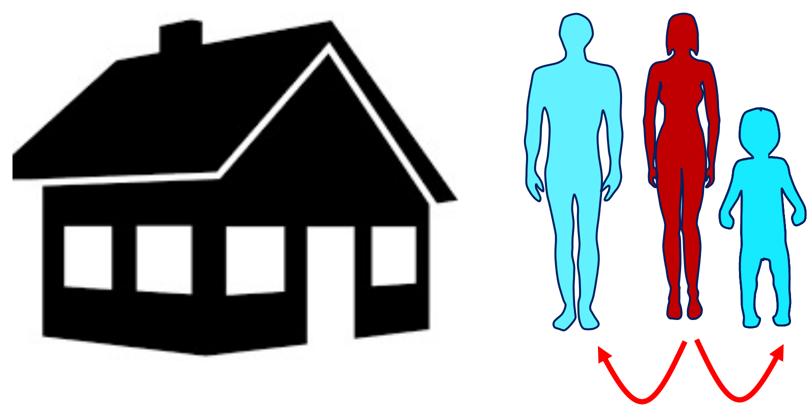
FRED Daily Dynamics

Location and size of each school



Household size, ethnicity, ages, income

Location and size of each workplace



The New FRED: Easier Population Modeling

- No computer programming required
- You can focus on scientific effort (e.g. data collection, conceptual modeling, experimental design)
- You define (declare) all concepts of interest, rules for agents, environmental resources, initial conditions, and simulation parameters
- FRED processes the declarations, sets up the population, applies initial conditions, simulates the activities and interactions of the agents, and tracks all user-defined conditions within the population
- FRED outputs reports, charts, and visualizations
- FRED provides a simple workflow environment for you and manages all the data produced by the simulation and associated metadata

How to Model with FRED

1. Decide if FRED is suited to your research problem
2. Conceptual modeling
3. Create rules for individuals
4. Create and run FRED Model
5. Revise model and repeat

Decide if FRED is suited to the research problem

- FRED is well-suited for
  - Population-level phenomena arising from individual interactions
  - Phenomena with a straightforward "Natural History"
  - Phenomena with strong social determinants
  - Phenomena with strong spatial characteristics
  - Problem dependent on longitudinal demographic projections

- FRED is less well-suited for
  - Detailed physiological modeling
  - Problems associated with detailed interactions among small groups (e.g. resolution of domestic conflicts)
  - Problems depending on high-resolution motion (e.g. traffic models)

Decide if FRED is suited to the research problem

Do you need this?

FRED

Or this?

NetLogo

Conditions in FRED

- *Conditions* are patterns of interest defined over a population

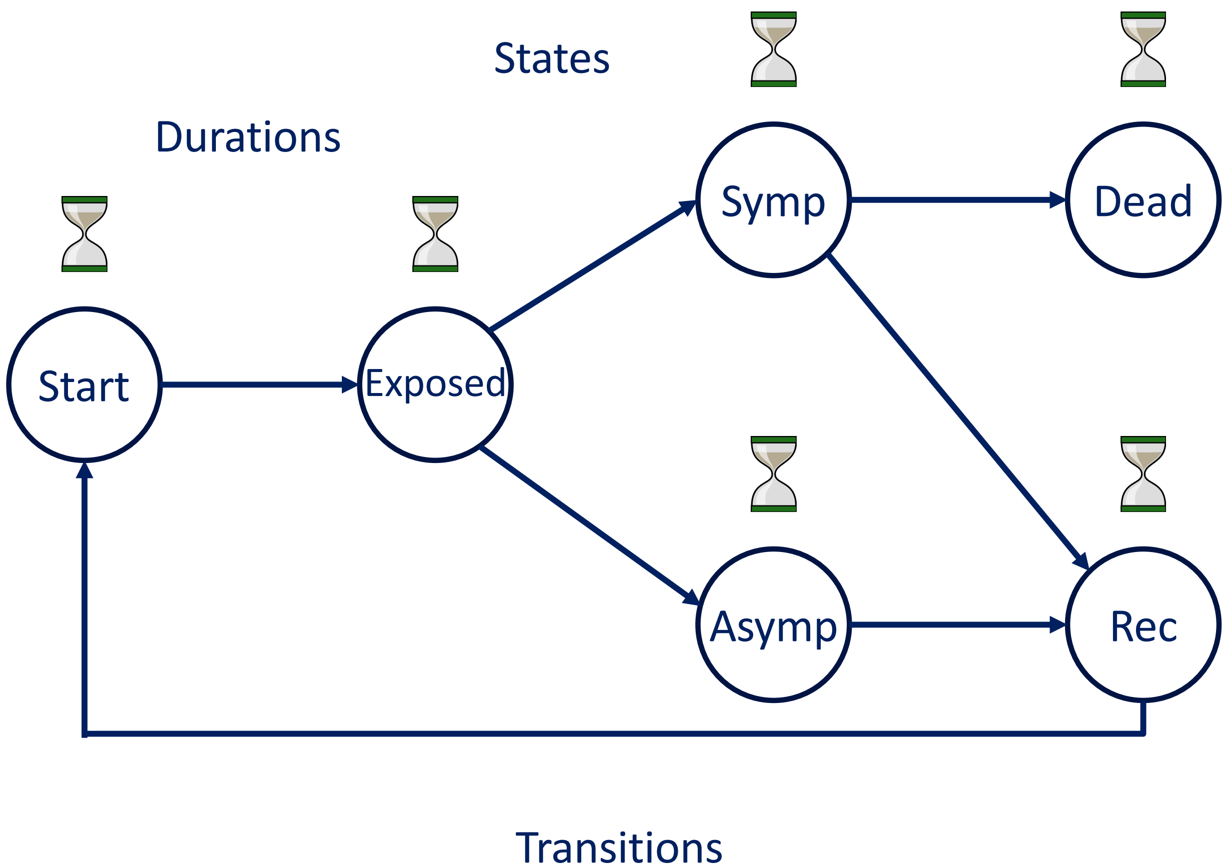
Examples

- Demographic conditions
  - maternity, mortality
- Health-related behaviors
  - vaccine acceptance and uptake, condom use, personal hygiene, exercise, violence, compliance, care-giving
- Social conditions
  - income inequality, access to insurance, gang activity, community activism, gun ownership
- Infectious diseases
  - flu, measles, dengue, chikungunya, HIV, HepC
- Noninfectious diseases
  - CVD, asthma, alzheimers, drug use disorder, obesity

Conditions and States

- You can define any number of conditions
- Each condition has a user-defined set of *states*
  - Conditions and states can have whatever names you choose
- Each agent is in exactly one state associated with each condition
  - The first named state is the initial state for each agent
- You define the duration of each state
  - Selected from statistical distribution or changed by side effect
- You provide rules for changing states
  - Logistic regression for probability of changing to any other state
- State can have health side effects
  - Transmissibility, susceptibility, symptoms, mortality, maternity
- States can have social contact side effects
  - Absent from school or work, isolation, hospitalization, etc.
- States can have side effects on other conditions

Condition = Influenza



Duration of States

- For every condition, each agent has a *current state*
- For every condition, each agent has at most one *scheduled state transition*
- When a state transition time arrives, the *transition matrix* is used to select the agent's *next state*
- You define the state durations and the state transitions

Duration of States

- How long before an agent changes state?

Distribution	Parameters	Use
normal	mean, std	produced by many small effects acting additively and independently e.g., human gestation period
lognormal	median, dispersion	produced by multiplication many effects, each of which is positive e.g., duration of illness, length of marriage before divorce
geometric	mean (mean = 1.0/p)	time before success of Bernoulli trials with prob p. e.g., time before winning a lottery
uniform	min, max	e.g., value of a dice toss

- Transient states
  - States with duration 0
- Absorbing states have infinite duration
  - examples: Death, Race, Male/Female (in models without Transgenders)
- Dormant states
  - States that FRED doesn't need to track (for efficiency)

Example: Pandemic Influenza Natural History

The states are: Susceptible, Exposed, Infectious, and Recovered

Rules:

1. People start out susceptible and remain susceptible until they are infected (that is, exposed).
2. People who are exposed become infectious after about 1-3 days.
3. People who are infectious recover after about 3-8 days.
4. Infectious people have moderate symptoms and stay home about 50% of the time.
5. Once recovered, people remain immune.

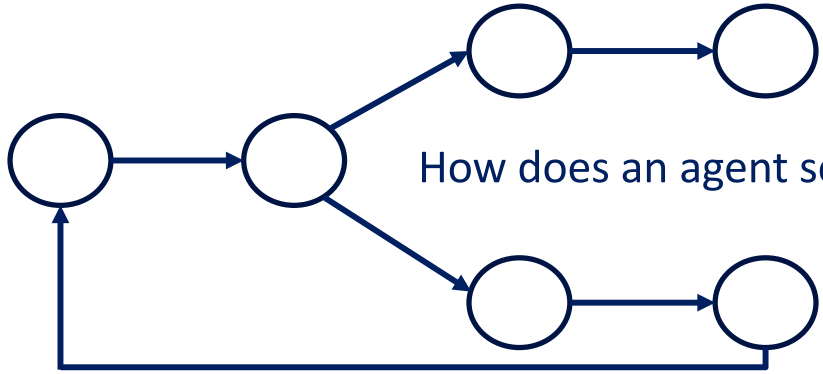
FRED Sample Condition File

```
INFLUENZA.states = Susceptible Exposed Infectious Recovered

# TRANSMISSION
INFLUENZA.transmission_mode = respiratory
INFLUENZA.transmissibility = 1.0

# RULE 1
INFLUENZA.Susceptible.susceptibility = 1.0
INFLUENZA.exposed_state = Exposed

# RULE 2 (from Lessler, 2009)
INFLUENZA.Exposed.duration_distribution = lognormal
INFLUENZA.Exposed.duration_median = 1.9
INFLUENZA.Exposed.duration_dispersion = 1.51
INFLUENZA.transition[Exposed][Infectious] = 1

# RULE 3 (Citation?)
INFLUENZA.Infectious.transmissibility = 1.0
INFLUENZA.Infectious.duration_distribution = lognormal
INFLUENZA.Infectious.duration_median = 5.0
INFLUENZA.Infectious.duration_dispersion = 1.5
INFLUENZA.transition[Infectious][Recovered] = 1

# RULE 4
INFLUENZA.Infectious.symptoms = moderate
INFLUENZA.Infectious.probability_of_household_confinement = 0.5
```

FRED Sample Condition File

```
# RULE 5
INFLUENZA.Recovered.is_dormant = 1

#########################################

# SIMULATION SETUP

# DURATION
days = 100

# POPULATION
locations_file = locations.txt

# CONDITIONS
conditions = INFLUENZA

# IMPORT CASES
INFLUENZA.import_file = import_influenza.txt

# VISUALIZATION
enable_visualization_layer = 1
INFLUENZA.Exposed.visualize = 1
INFLUENZA.Infectious.visualize = 1
INFLUENZA.Recovered.visualize = 1
```

Transition Rules



How does an agent select the next state?

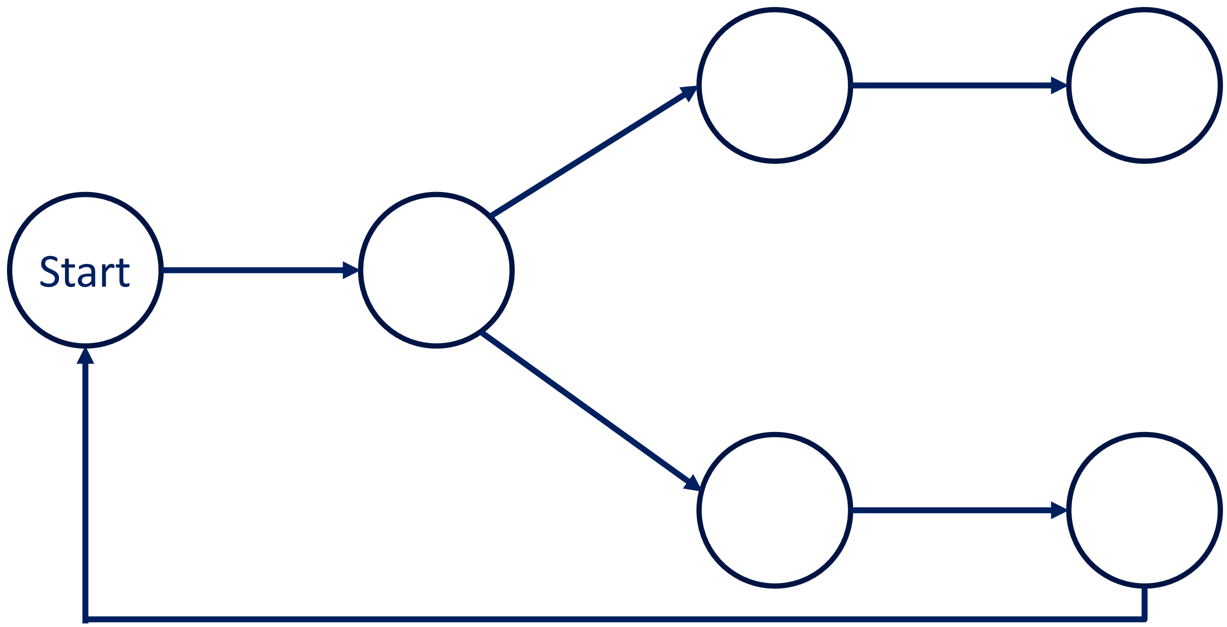
State Transition Matrix

	Next State		
State	**A**	**B**	**C**
A	0.0	0.5	0.5
B	0.1	0.8	0.1
C	0.0	0.0	1.0

To select next state:

1. Compute probabilities in row of current state
2. Select next state using the distribution

FRED Transition Rules



Rules can be:

- Logic-driven
- Probability-driven
- Event-driven

Factors that can affect an agent's state

Social determinants:

- Demographics: age, race, sex, number of children
- Household: location (state, county or census tract), size, income
- Workplace or school: location, size
- Activity profile: pre-school, student, employed, retired, prisoner, military, nursing home resident, dorm resident

Agent's own state

- Current health states: active conditions, immunity status, infection status, symptoms, where exposure occurred

Other People's States

- Current epidemic levels of any user-defined condition in the population or in my mixing groups

Environmental States

- Time: year, month, day of week

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FRED Built-in Risk Factors

SOCIAL DETERMINANTS

age
age_squared
log_of_age
age_is_<a> = 0.0 for a in {0,110}
age_is_<a>+ = 0.0 for a in {0,110}
age_is_<a>-<b> for a in {0,5,...,110}
and b in {a+4,a+9,...}
is_female
is_male
race_is_white
race_is_nonwhite
race_is_african_american
race_is_american_indian
race_is_alaska_native
race_is_tribal
race_is_asian
race_is_hawaiian_native
race_is_other
race_is_multiple
has_household_income_in_first_quartile
has_household_income_in_second_quartile
has_household_income_in_third_quartile
has_household_income_in_fourth_quartile
has_household_income_below_median
has_household_income_above_median
household_size_is_1
household_size_is_2
household_size_is_3
household_size_is_4
household_size_is_5
household_size_is_6
household_size_is_7
household_size_is_8
household_size_is_9
household_size_is_10+
is_resident_in_group_quarters
is_resident_in_college_dorm
is_resident_in_nursing_home
is_resident_in_military_barracks
is_resident_in_prison

SOCIAL DETERMINANTS (cont'd)

is_student
is_employed
is_unemployed
is_retired

number_of_children_is_0
number_of_children_is_1
number_of_children_is_2
number_of_children_is_3
number_of_children_is_4
number_of_children_is_5
number_of_children_is_6+

state_fips_is_NN
county_fips_is_NNNNN
census_tract_fips_is_NNNNNNNNNNN

household_threshold_exceeded
household_threshold_not_exceeded
neighborhood_threshold_exceeded
neighborhood_threshold_not_exceeded
school_threshold_exceeded
school_threshold_not_exceeded
workplace_threshold_exceeded
workplace_threshold_not_exceeded

ENVIRONMENTAL STATES

year_is_2000
...
year_is_2100
log_current_year
month_is_january
..
month_is_december
day_of_week_is_sunday
...
day_of_week_is_saturday
is_weekday
is_weekend

PERSONAL STATES

is_in_state_COND.STATE
was_ever_exposed_to_COND
has_symptoms_of_COND
is_transmissible_for_COND
exposed_to_COND_in_household
exposed_to_COND_in_neighborhood
exposed_to_COND_in_school
exposed_to_COND_in_workplace

OTHER PEOPLE'S STATES

any_others_in_household_in_state_COND.STATE
any_others_in_neighborhood_in_state_COND.STATE
any_others_in_school_in_state_COND.STATE
any_others_in_workplace_in_state_COND.STATE

log_of_number_in_household_in_state_COND.STATE
log_of_number_in_neighborhood_in_state_COND.STATE
log_of_number_in_school_in_state_COND.STATE
log_of_number_in_workplace_in_state_COND.STATE

incidence_threshold_exceeded_for_state_COND.STATE
prevalence_threshold_exceeded_for_state_COND.STATE
cumulative_threshold_exceeded_for_state_COND.STATE

log_of_incidence_count_for_state_COND.STATE
log_of_prevalence_count_for_state_COND.STATE
log_of_cumulative_count_for_state_COND.STATE

Logic-driven State Transitions

- You can assign transition probabilities based on *any logical combinations of the factors*
  - FRED is *propositionally complete*, meaning that you can control state transitions based on any combination of IF-THEN-ELSE, AND, OR, and NOT statements

- This often involves transient (duration = 0) states as intermediary states

Asthma prevalence

Age	White		Nonwhite	
	Male	Female	Male	Female
0-4	3.7	3.7	11.5	9.0
5-14	9.5	8.4	20.1	17.7
15-19	9.4	11.2	12.8	17.9
20-24	6.5	11.5	14.3	13.2
25-34	6.5	10.5	8.8	12.5
35-64	5.9	10.7	6.3	12.7
65+	5.5	7.5	7.8	7.9

Source: National Health Interview Survey, National Center for Health Statistics, CDC

To use this in FRED:

1. Write rules to separate the population into the given subgroups
2. Assign the condition risk according to the given prevalence

Logic-driven State Transitions

```
conditions = GROUP ASTHMA

GROUP.states = Start Female Male WhiteF WhiteM NonwhiteF NonwhiteM WhiteF0-4 ...

GROUP.Start.duration = 0
GROUP.transition[Start][Female].is_female = 1
GROUP.transition[Start][Male].is_male = 1

GROUP.Female.duration = 0
GROUP.transition[Female][WhiteF].race_is_white = 1
GROUP.transition[Female][NonwhiteF].race_is_nonwhite = 1

GROUP.WhiteF.duration = 0
GROUP.transition[WhiteF][WhiteF0-4].age_is_0-4 = 1
GROUP.transition[WhiteF][WhiteF5-9].age_is_5-9 = 1
...
```

Probability-driven State Transitions

Traditional Transition Matrix

	Next State		
State	**A**	**B**	**C**
A	0.0	0.5	0.5
B	0.1	0.8	0.1
C	0.0	0.0	1.0

Challenges:

- Make transitions more individualized
- Take into account dynamic aspects
- State space explosion

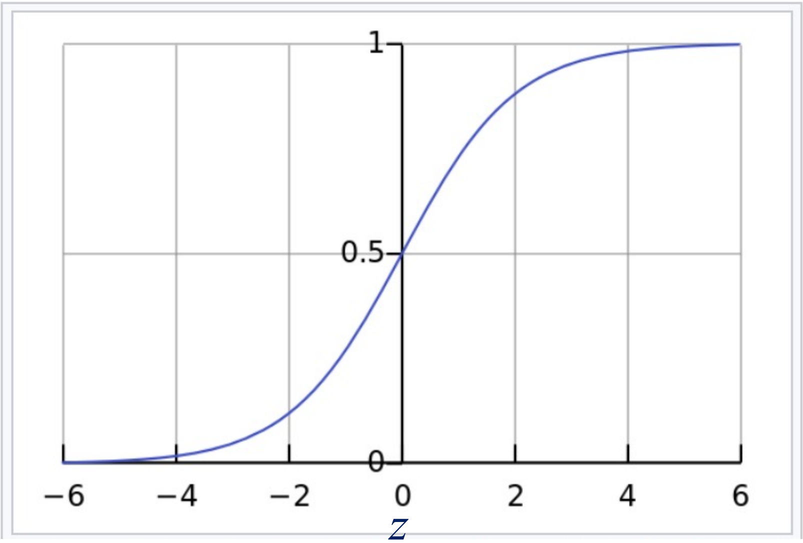
Probability-driven State Transitions

```
conditions = GROUP ASTHMA

GROUP.states = Start Female Male WhiteF WhiteM NonwhiteF NonwhiteM WhiteF0-4 ...

GROUP.Start.duration = 0
GROUP.transition[Start][Female].is_female = 1
GROUP.transition[Start][Male].is_male = 1

GROUP.Female.duration = 0
GROUP.transition[Female][WhiteF].race_is_white = 1
GROUP.transition[Female][NonwhiteF].race_is_nonwhite = 1

GROUP.WhiteF.duration = 0
GROUP.transition[WhiteF][WhiteF0-4].age_is_0-4 = 1
GROUP.transition[WhiteF][WhiteF5-9].age_is_5-9 = 1
...

ASTHMA.states = Start AtRisk None
ASTHMA.Start.duration = 0
ASTHMA.transition[Start][AtRisk].is_in_state_GROUP.WhiteF0-4 = 0.037
ASTHMA.transition[Start][None].is_in_state_GROUP.WhiteF0-4 = 0.963
```

Logistic Regression

$\sigma(z) = 1 / (1 + \exp(-z)$ and $z = \beta_0 + \beta_1 * x_1 + \beta_2 * x_2 + \ldots + \beta_n * x_n$

coefficient (β_1) — risk factor (x_1)



Wikipedia

Standard logistic regression function $\sigma(z)$.
Note that $\sigma(z)$ returns a value (0, 1) for all z.

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Probability-driven State Transitions

FRED Transition Matrix

	Next State		
State	**A**	**B**	**C**
A	$\alpha(z_{AA})$	$\alpha(z_{AB})$	$\alpha(z_{AC})$
B	$\alpha(z_{BA})$	$\alpha(z_{BB})$	$\alpha(z_{BC})$
C	$\alpha(z_{CA})$	$\alpha(z_{CB})$	$\alpha(z_{CC})$

Each entry has its own set of coefficients.

To select next state:

1. Compute probabilities in row of current state
2. Normalize
3. Select next state using the distribution

Probability-driven State Transitions

(with thanks to Hawre)

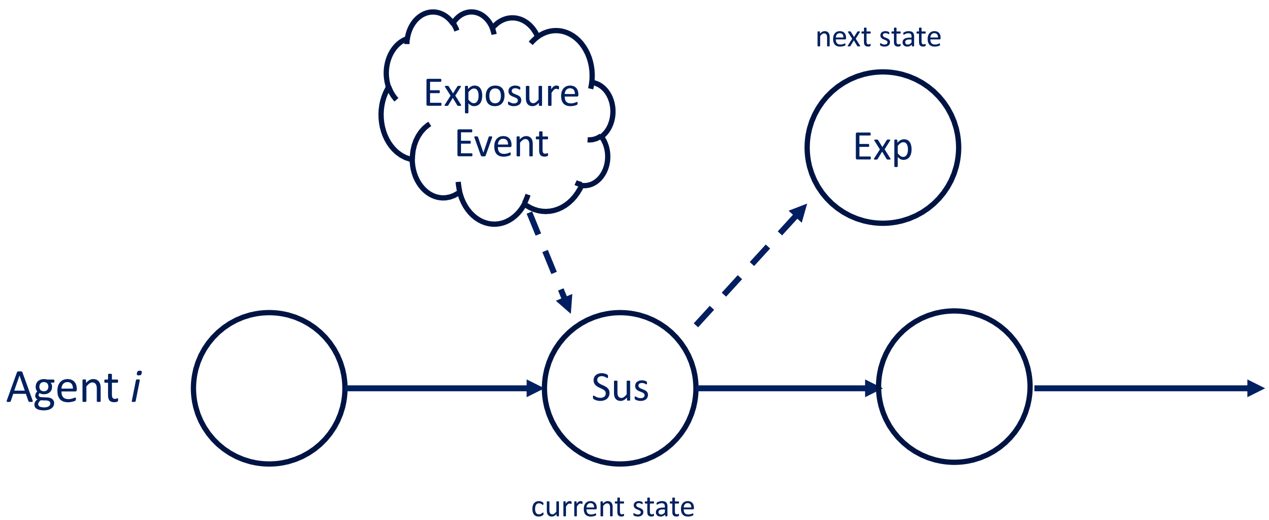
The probability of heroin use onset is described by:

$$\text{Prob(Heroin)} = 1 / (1 + \exp(-z))$$

where $z = -214.8 + 0.112 * \text{age} - 0.00151 * \text{age}^2 - 0.18 * \text{female} + 1.89 * \text{po} + 2.447 * \text{cocaine} + 0.979 * \text{meth} + 1.256 * \text{mj}$

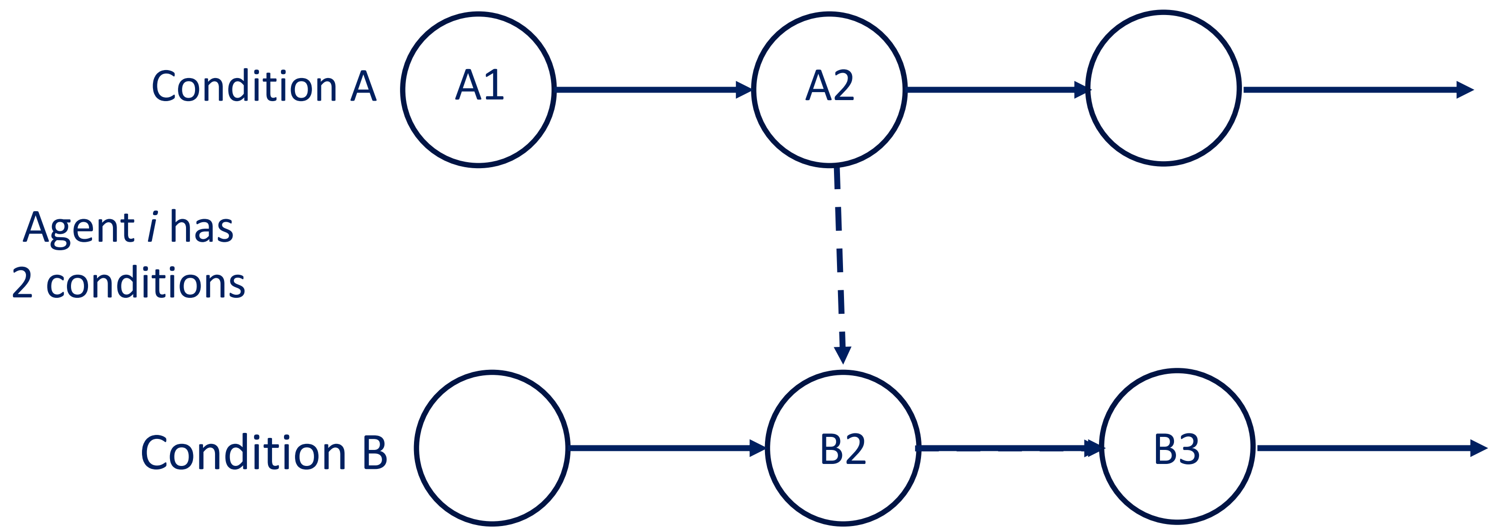
```
conditions = HEROIN PO COCAINE METH MJ
HEROIN.states = NonUse Use ProblemUse
HEROIN.duration = 30
HEROIN.transition[NonUse][Use].coeff = -214.8
HEROIN.transition[NonUse][Use].age = 0.112
HEROIN.transition[NonUse][Use].age_squared = -0.00151
HEROIN.transition[NonUse][Use].is_female = -0.18
HEROIN.transition[NonUse][Use].is_in_state_PO.Use = 1.89
HEROIN.transition[NonUse][Use].is_in_state_COCAINE.Use = 0.979
HEROIN.transition[NonUse][Use].is_in_state_MJ.Use = 1.256
```

Event-driven State Transitions (Part 1)



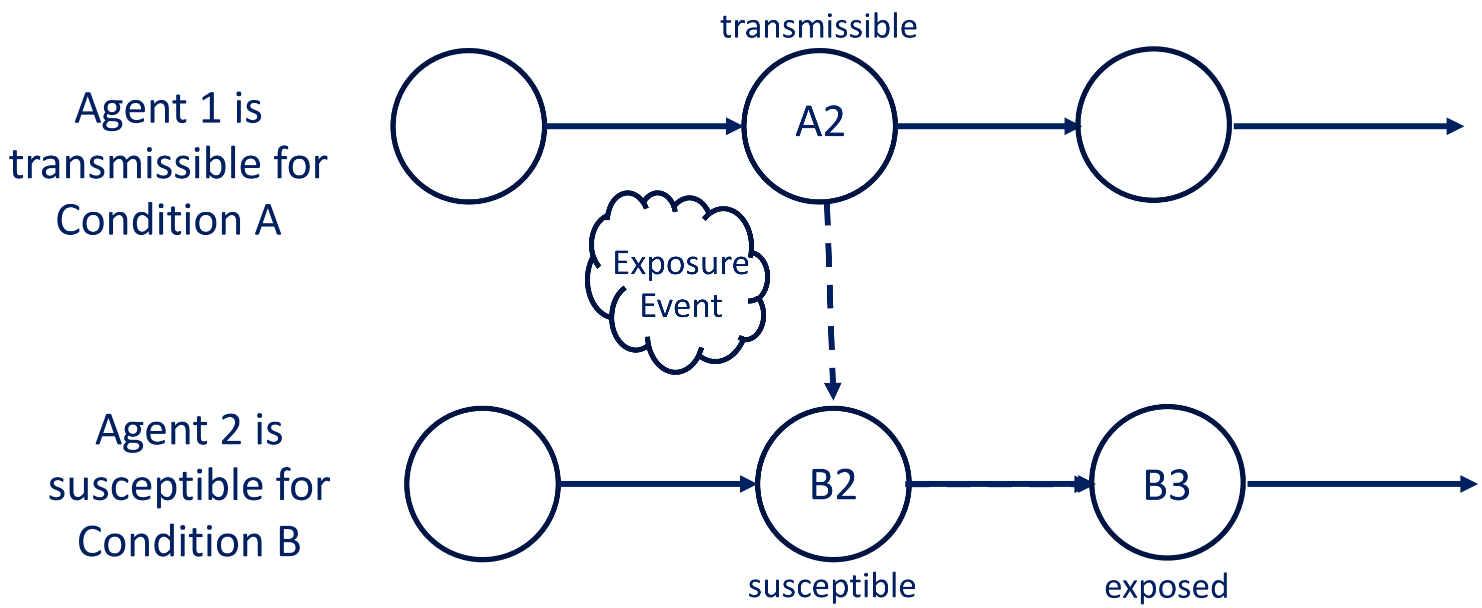
- Agents can be exposed to any condition through simulation events
  - *interaction with another agent who is transmissible for this condition*
  - *imported cases caused by an unidentified source*
- User defines the schedule of imported cases: day, location, quantity
- Agents must be in a susceptible state to be exposed

Event-driven State Transitions (Part 2)



- When an agent enters a state, it can have a *side effect* on a state in another condition, causing the agent to change to a different state
- Example: when a person in a VACCINATION condition changes from state *Received* into the *Success* state, that person changes its state in the INFLUENZA condition from *Susceptible* to *Immune*

Event-driven State Transitions (Part 3)



- We can tell FRED that Condition A causes exposure to Condition B
- If agent 1 "transmits" to agent 2, then agent 2 is exposed to condition B
- Examples:
  - drug dealer sells to drug user
  - perpetrator inflicts violence on victim
  - offspring inherits wealth from parent

Event-driven State Transitions (Part 3)

```
conditions = PERPETRATOR VICTIM
PERPETRATOR.states = Start Inactive Active Arrested
VICTIM.states = Safe AtRisk Injured Recovered Dead
...
# Condition Properties
PERPETRATOR.transmission_mode = proximity
PERPETRATOR.transmissibility = 0.01
...
VICTIM.exposed_state = Injured
...
# State Properties
PERPETRATOR.Active.transmissibility = 1.0
PERPETRATOR.Active.condition_to_transmit = VICTIM
...
VICTIM.AtRisk.susceptibility = 1
```

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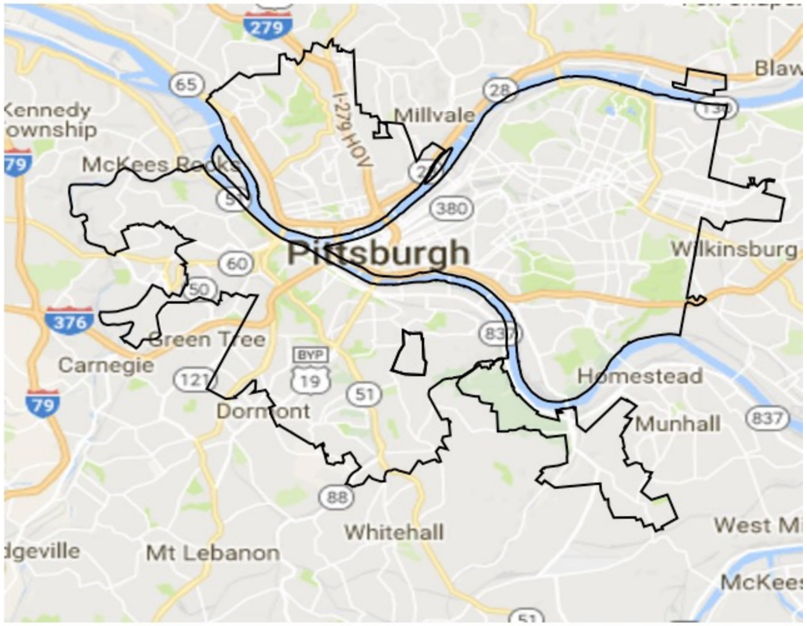
Plots and Visualization

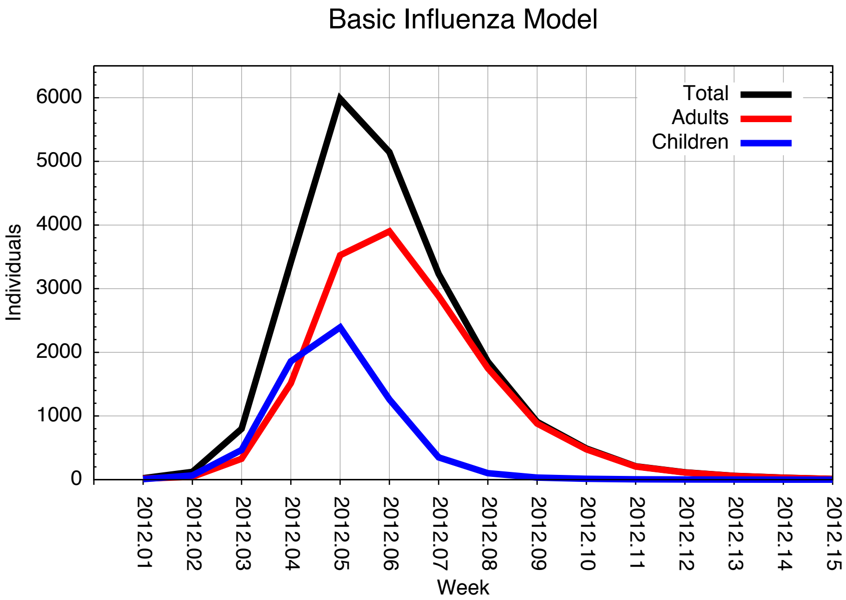
- FRED can produce time plots and movies for *any condition and state*

FRED Simulation of EMS Requests
Severity Level 5

2025-08-24



Blue = Asthma Attacks   Red = Heat Stroke   Black = All EMS Calls



Environmental Resources

- You can define any number of *environmental resources*
  - e.g., pharmacies, clinics, vaccine doses, treatment beds, bags of heroin, cooling centers
- You declare the resources properties:
  - timing (days available)
  - location (lat-lon)
  - quantity (count or per capita)
- You can declare that an agent must be able to access a resource to enter a given state
  - how far can the agent travel
  - how many resources are needed?
  - does the agent return the resources when entering another state?

```
resources = BAGS
BAGS.import_file = delivery_schedule.txt

HEROIN.Use.resource = BAGS
HEROIN.Use.resource_required = 1
HEROIN.Use.resource_returned = 0
HEROIN.Use.resource_distance = 10.0
```

Near-term Plans

- FRED Web interface
  - wizards to help you define new conditions
  - setup experiments
  - run FRED experiments
  - create reports (csv files), plots and movies
  - save your work
- FRED community
  - shareable condition definitions
  - shareable models on the web site
  - wiki
- FRED training and documentation
  - Using FRED Web
  - Plotting and Visualization Tools
  - Library of simple models
  - Calibration Methods
  - Sensitivity and Uncertainty Analysis
  - Book?

Condition Properties

```
# State definitions
COND.states = state_1 state_2 ... state_n
COND.maternity_state = none | <state_name>
COND.fatal_state = none | <state_name>

# Transmission
COND.transmission_mode = none | proximity | environmental |
                         respiratory | sexual | vector
COND.transmissibility = 0.0
COND.exposed_state = none | <state_name>
COND.import_file = none

# Transitions
COND.transition[state_i][state_j] = 0.0
COND.transition[state_i][state_j].coeff = 0.0
COND.transition[state_i][state_j].RISK_FACTOR = 0.0
COND.transition[state_i][state_j].RISK_FACTOR.coeef = 0.0
...
# Reporting
COND.enable_health_records = 0
```

State Properties (1)

```
# Duration
COND.STATE.duration_distribution = normal | lognormal |
                              exponential | uniform
COND.STATE.duration_mean = -1.0
COND.STATE.duration_stdev = 0.0
COND.STATE.duration_median = -1.0
COND.STATE.duration_dispersion = 1.0
COND.STATE.duration_mean = -1.0
COND.STATE.duration_lower_bound = 0.0
COND.STATE.duration_upper_bound = 99999.0
COND.STATE.duration_offset = 0.0

# Transition
COND.STATE.is_dormant = 0
COND.STATE.default_next_state = <current state>

# Resources
COND.STATE.resource = none
COND.STATE.resources_required = 0
COND.STATE.resource_distance = -1
# Visualization
COND.STATE.visualize = 0
```

State Properties (2)

```
# Health side effects
COND.STATE.susceptibility = 0.0
COND.STATE.transmissibility = 0.0
COND.STATE.condition_to_transmit = COND2
COND.STATE.symptoms = none | mild | moderate | severe

# Contact side effects
COND.STATE.probability_of_household_confinement = 0.0
COND.STATE.decide_household_confinement_daily = 0
COND.STATE.probability_absent_from_household = 0.0
COND.STATE.probability_absent_from_neighborhood = 0.0
COND.STATE.probability_absent_from_work = 0.0
COND.STATE.probability_absent_from_school = 0.0
COND.STATE.probability_of_isolation = 0.0
COND.STATE.probability_of_hospitalization = 0.0
COND.STATE.probability_of_visiting_outpatient_clinic = 0.0

# Side effects on other Conditions
COND.STATE.multiply_susceptibility_to_COND2_by = 1.0
COND.STATE.multiply_transmissibility_of_COND2_by = 1.0
COND.STATE.multiply_symptoms_of_COND2_by = 1.0
COND.STATE.change_state_from_COND2.STATE2_to = STATE3
```

Summary

- FRED is a unique tool for social science modeling
- Agents in FRED can have any number of conditions and can change states based on a variety of interactions with other agents and with the environment
- FRED requires no computer programming skills to define complex agent based models
- FRED requires a systems thinking approach to identify conditions of interest, their states, and the rules for changing states

Enjoy!

FRED Resources

- FRED Web:

  http://fred.publichealth.pitt.edu

- FRED Github:

  https://github.com/PublicHealthDynamicsLab/FRED

- FRED Team:

  John Grefenstette
  David Galloway
  Mary Krauland
  Bob Frankeny
  Mike Lann
  David Sinclair

[redacted]

PITT PUBLIC HEALTH

FRED Architecture