Mathematical Modeling for Comprehensive HIV Prevention Planning I:

MARDHAM—
Exploring the drivers of racial disparities in HIV among MSM

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In conjunction with

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The Statnet Development Team

Modeling intro

- What is modeling?
  - The simulation of an epidemic—typically through time—according to a set of assumptions
- What kind of assumptions?
  - behavioral, clinical, virological, demographic, etc.
- What defines a good model?
  - One that provides novel clarity about a question of epidemiological or clinical relevance
  - One in which the assumptions are well grounded in empirical data
- Why modeling?

Modeling intro

- Imagine a really simple infection
  - One can acquire it through *contact* with someone who is already infected
  - One cannot recover from it
  - Those who are infected have a mortality rate 10 times higher than everyone else
  - When a negative person and a positive person have contact, there is a 2% probability of transmission
  - In our population of interest, people have on average 0.6 contacts per month
  - Contacts occur randomly and independently
  - Prevalence starts out at 1 person infected out of 1000.
- Where does the epidemic lead?
- Now, what if we convince everyone to use protection 16% of the time? Now where does it lead?

Modeling intro

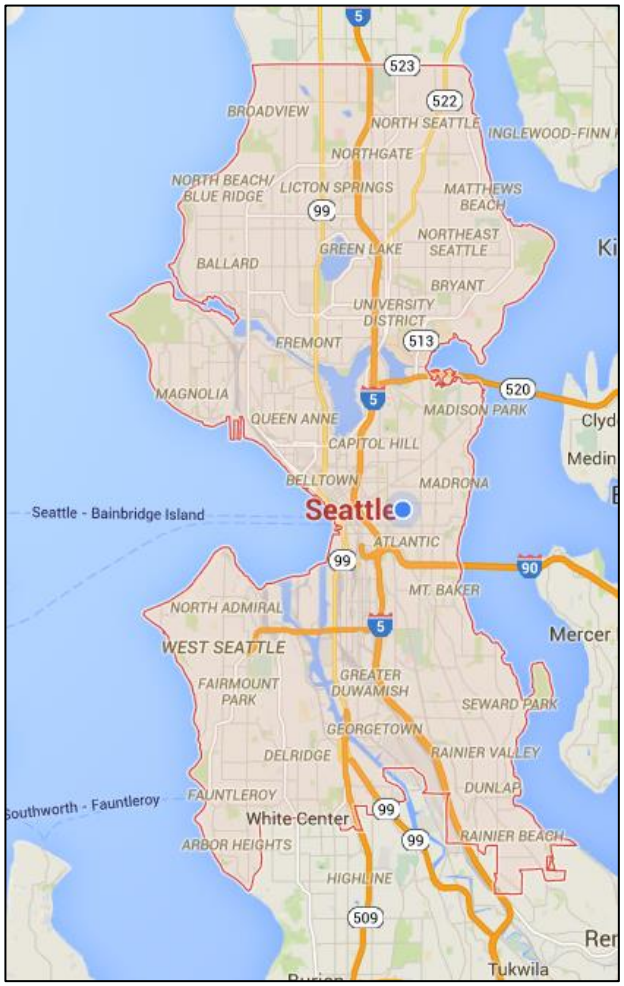
- If this were a model of HIV….

  - **Its behavioral assumptions would be overly simplistic. In reality:**
    - Most contacts occur in the context of persistent partnerships
    - Not everyone has the same number of partners/contacts
    - People don't choose their partners randomly
    - People change their behavior for many reasons (e.g. after testing positive)

  - **Its biological and clinical assumptions would be overly simplistic. In reality:**
    - Not all discordant contacts are equally likely to transmit (e.g. stage of infection, treatment, circumcision, PrEP)
    - Not everyone who is infected is equally likely to die (disease progression occurs)

  - **Etc.**

Models are like maps



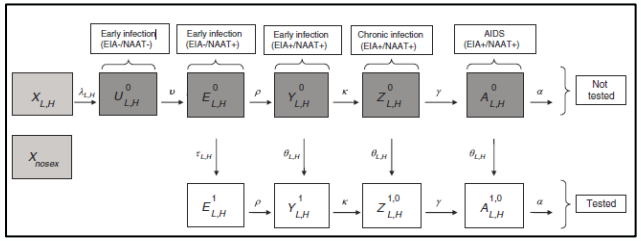
- they are abstractions
- they have specific purposes
- they have scale
- they must balance realism with understandability

Some purposes of models in HIV

- To understand theoretical impact of different phenomena on epidemic outcomes
- To understand the origins and maintenance (and sometimes reduction) of disparities
- To predict future HIV incidence and prevalence in a population
- To predict the likely impact of a particular intervention or combination of interventions in a population

Existing epidemic modeling work

- Traditionally done mostly by biologists, zoologists, applied mathematicians, physicists

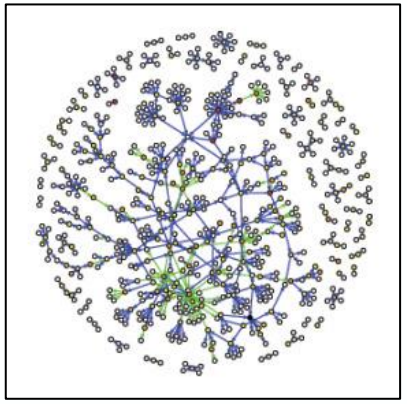


- Mostly uses "compartmental models"
  - Based in differential equations
  - Represents people only in the aggregate
  - Has a variety of practical restrictions on how complex the models can get
  - Cannot represent some phenomena of crucial importance to some questions

- Tends to focus more on biological and clinical realism than behavioral realism

UW Network modeling group

- Part of a growing effort to use “network” models in HIV modeling



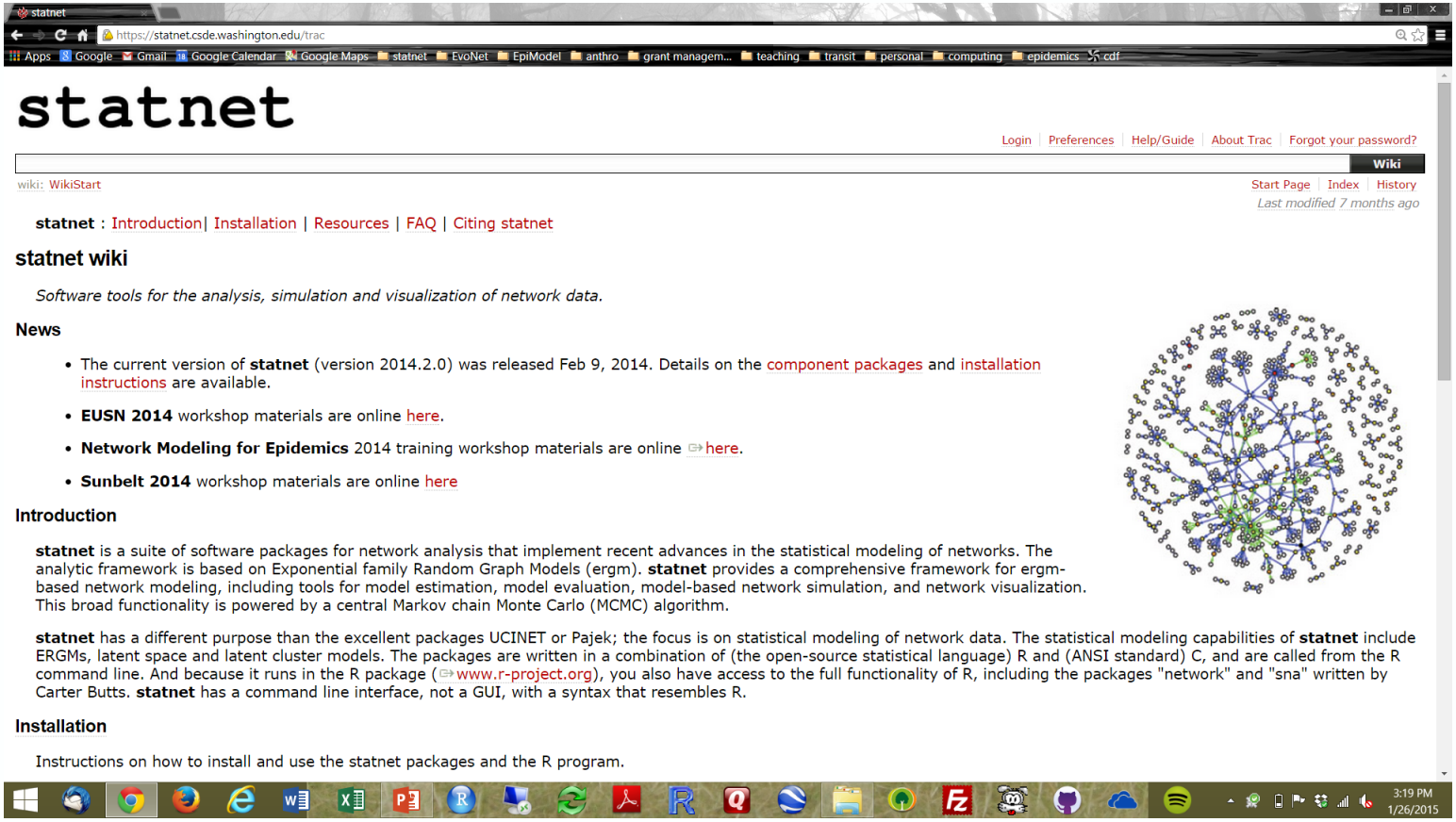
  - Represents all individuals in a simulated population explicitly
  - Represents the evolving sexual networks among them explicitly as well
  - More prevalent among social scientists and statisticians
  - More challenging, but also much more flexible

    - can model important phenomena that compartmental models can’t
    - can model many more phenomena at once
    - are crucial for complex combination prevention

UW Network modeling group

- Work on increasing the collection of relational network data in HIV behavioral and prevention studies
- Work on developing new methods and software for the analysis of network data and for network modeling
- Work locally, domestically and internationally

UW Network modeling group



Steve's niche: MSM projects

Name of Project	Modeling aim	Population modeled
PUMA	Tailoring combination HIV prevention for MSM in the Americas	MSM in major metro areas in the US and Peru
Metromates	Considering potential impact of HIV testing strategies for MSM	MSM in Southern California
SMS	Using network structure to target peer-led HIV interventions	MSM in Hyderabad, India
EvoNet	Understanding the effects of network structure on viral evolution	Many, TBD
MARDHAM	**Explaining racial disparities in HIV in young MSM**	**Young Black and White MSM in metro Atlanta**

MARDHAM

- Modeling Approaches to Racial Disparities in HIV among Atlanta MSM
- Seeks to answer why we are seeing such large racial disparities in HIV incidence among young MSM
- Uses data from three existing network studies collected by Emory researchers (each developed with input from CAB and Black MSM and Young MSM focus groups in ATL)
- Funded by NIH R21

Black/White disparities in HIV among US MSM

- **At times astounding:**
  - **12**% annual incidence in ATL YBMSM (Rosenberg 2014)
  - **3**% annual incidence in Black MSM (HPTN-061)
  - White MSM typically a little less than **1%**
  - King County: Blacks = 7% of pop; 10% of MSM HIV diagnoses
- **A public health priority** — US National HIV/AIDS strategy: 1 of 4 main goals is "Reducing HIV-Related Disparities and Health Inequities"
- **Not easy to explain** — study after study show equal or fewer # of partners / amount of UAI among Black MSM than White MSM
- **Some disparity is old** — CDC: 26% PLWA prior to 1987 were Black (Blacks 12% of pop)
- **Also true of other STIs**
  - Rosenberg 2014: Black/White MSM incidence =
    - ~ 2 x (chlamydia, rectal gonorrhea)
    - ~ 10 x (urethral gonorrhea)
    - infinite (syphilis 6% vs 0% incidence)
- **Also true in heterosexuals**
- **Found in communities of various sizes and compositions**

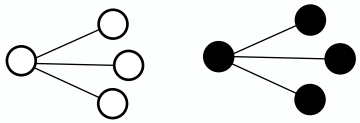
Potential origins and areas for intervention

Numerous great meta-analyses on this; many by Millett and colleagues

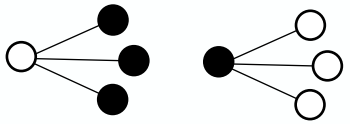
• **Poverty, stigma, racism, incarceration, homophobia**	Undoubtedly yes, as upstream factors. But what are the causal pathways, given the similarities in many intervening measures?
• **Assortative mixing by race:**	clearly a necessary piece, but only the start
• **Population size:**	smaller populations can more easily generate concentrated epidemics under some conditions. But not always, plus Atlanta is close to 50/50
• **Later diagnosis:**	clearly a piece, but data are highly conflicted
• **Less disclosure:**	a clear difference (e.g. 45% Black, 69% White in one-time AI contacts), and affects effectiveness of sero-adaptive behaviors
• **Later and less effective treatment:**	also a clear difference (e.g. in MMP linkage to care in 3 months = 72% Black MSM, 83% White MSM). Less viral load suppression = more potential transmission to partners

Potential origins and areas for intervention

- **Concurrency** – not so clear a story here as it is for disparities among heterosexuals
  - e.g. Rosenberg et al 2012: no differences by race in **having** conc. partners



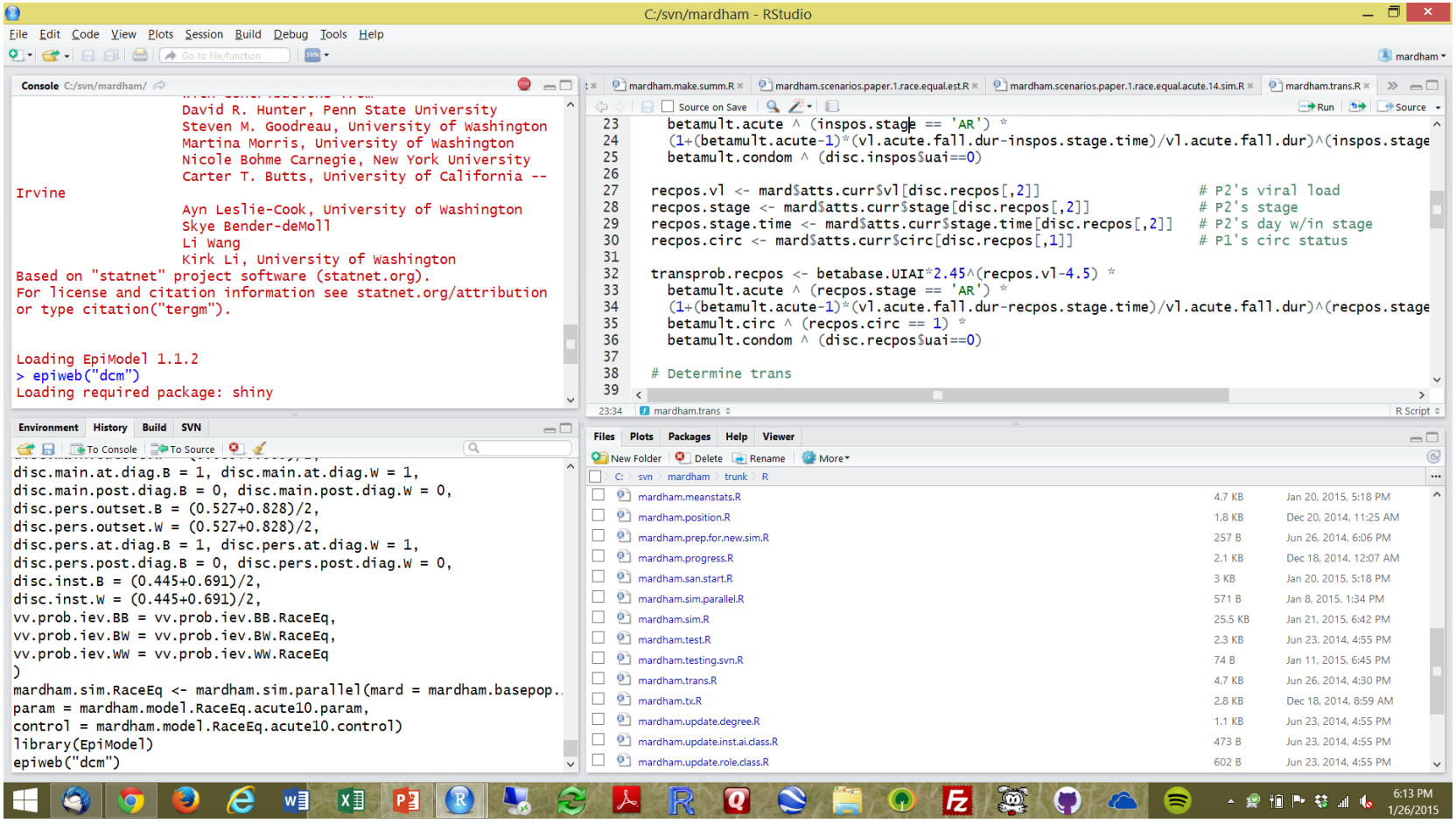
  - but Rosenberg et al 2013: some differences by race in **being** a conc. partner



- **Assortative mixing by age** – minor differences with Blacks having wider age gaps; can help perpetuate the virus through cohorts
- **Earlier initiation of UAI in main relationships** – potentially exposing more Black partners during acute infection?

Are the magnitude of these effects together enough to drive observed disparities?

MARDHAM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David R. Hunter, Penn State University
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Source on Save
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Source
23 betamult.acute ^ (inspos.stage == 'AR') *
24 (1+(betamult.acute-1)*(vl.acute.fall.dur-inspos.stage.time)/vl.acute.fall.dur)^(inspos.stage
25 betamult.condom ^ (disc.inspos$uai==0)
26
27 recpos.vl <- mard$atts.curr$vl[disc.recpos[,2]] # P2's viral load
28 recpos.stage <- mard$atts.curr$stage[disc.recpos[,2]] # P2's stage
29 recpos.stage.time <- mard$atts.curr$stage.time[disc.recpos[,2]] # P2's day w/in stage
30 recpos.circ <- mard$atts.curr$circ[disc.recpos[,1]] # P1's circ status
31
32 transprob.recpos <- betabase.UIAI*2.45^(recpos.vl-4.5) *
33 betamult.acute ^ (recpos.stage == 'AR') *
34 (1+(betamult.acute-1)*(vl.acute.fall.dur-recpos.stage.time)/vl.acute.fall.dur)^(recpos.stage
35 betamult.circ ^ (recpos.circ == 1) *
36 betamult.condom ^ (disc.recpos$uai==0)
37
38 # Determine trans
39
23:34 mardham.trans
R Script
Environment History Build SVN
To Console To Source
disc.main.at.diag.B = 1, disc.main.at.diag.W = 1,
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)
mardham.sim.RaceEq <- mardham.sim.parallel(mard = mardham.basepop..
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library(EpiModel)
epiweb("dcm")
Files Plots Packages Help Viewer
New Folder Delete Rename More
C: svn mardham trunk R
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MARDHAM Model – behavioral aspects

- Men have sex within three different contexts: main partnerships, casual (but persistent) partnerships, one-offs
- We have data on, and model, the "degree matrix" of ongoing partnerships (main and casual) by race, e.g.

Young White MSM

		Casual		
		0	1	2
Main	0	44%	18%	10%
	1	23%	3%	2%

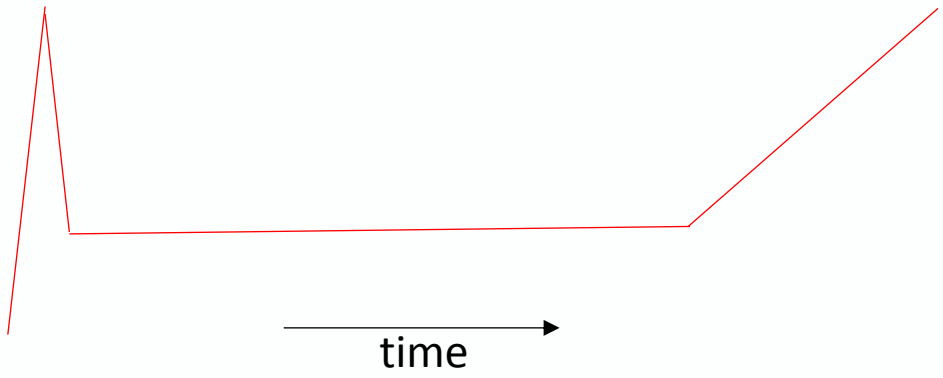
- Men also partner up according to patterns of race and age mixing observed in the data
- Within those relationships, men have AI at different frequencies, depending on the race combo (BB, BW, WW)
- Men also have AI one-offs at rates that depend on their race and their current main/casual partnership configuration

MARDHAM Model – behavioral aspects

- Men use condoms during AI at different rates depending on:
    - Race combo
    - Partner type
    - Diagnosis status (whether one or both is diagnosed positive)
    - Disclosure status (whether he tells his partner he's positive)
    - Viral suppression status
- Men have different sexual role preferences (from all receptive to all insertive)
- Some men never test for HIV; most do, at race-specific rates
- Some men never disclose to partners; most do, at race-specific rates
- Eventually: we will have additional metrics about concurrency by race of partner

MARDHAM Model – virological aspects

- In the absence of treatment, viral load (and infectiousness):



- Men initiate treatment
- Men achieve full or partial suppression
- Men halt treatment
- Men re-initiate treatment

} At race-specific rates

- Full and partial suppression each reduce transmissibility and increase survival

MARDHAM model overview

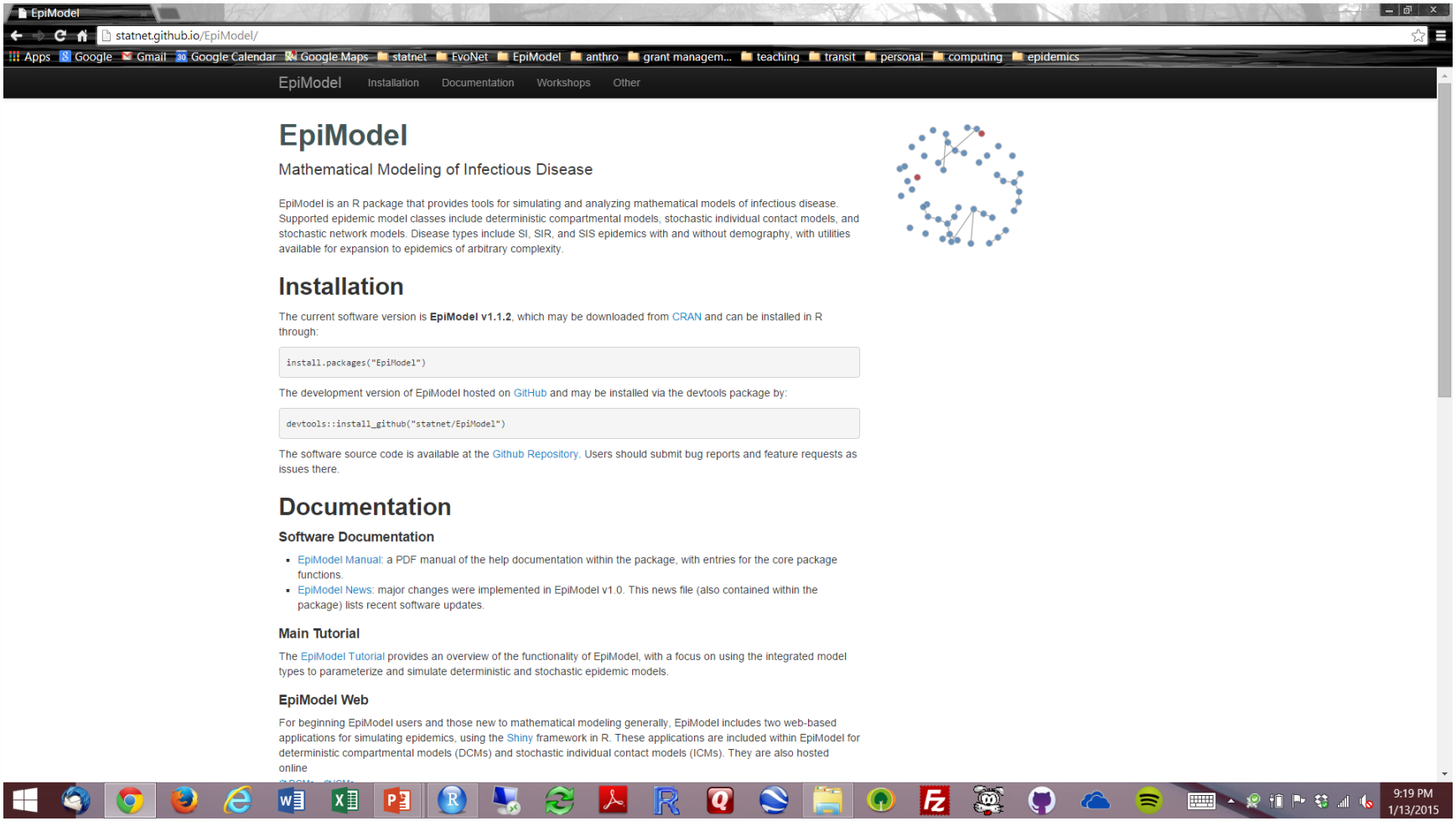
EACH TIME STEP

- Update demographics (arrivals, deaths, departures, aging)
- Update other attributes (viral load, testing, treatment, etc.)
- Evolve main and casual networks forward one time step
- Decide which main and casual partnerships involve AI
- Form that day's one-off AI network
- Simulate disclosure
- Simulate selection of role and condom use in each AI act
- Determine transmissions as fx of viral load, role, condom use
- Engage in large amounts of bookkeeping

MARDHAM model

- Model runs began two days ago!
  - So no results yet to show you
- With pre-existing data, this took:
  - 1.5 years to write model code
  - 1.5 years to conduct data analysis in ways necessary for model
- Reasons for time:
  - Complex network models are indeed time-consuming
  - Data that were collected for other purposes are often not parameterized in the way needed for models
  - EpiModel did not yet exist

EpiModel


EpiModel
statnet.github.io/EpiModel/
Apps Google Gmail Google Calendar Google Maps statnet EvoNet EpiModel anthro grant managem... teaching transit personal computing epidemics
EpiModel Installation Documentation Workshops Other
EpiModel
Mathematical Modeling of Infectious Disease
EpiModel is an R package that provides tools for simulating and analyzing mathematical models of infectious disease. Supported epidemic model classes include deterministic compartmental models, stochastic individual contact models, and stochastic network models. Disease types include SI, SIR, and SIS epidemics with and without demography, with utilities available for expansion to epidemics of arbitrary complexity.
Installation
The current software version is EpiModel v1.1.2, which may be downloaded from CRAN and can be installed in R through:
install.packages("EpiModel")
The development version of EpiModel hosted on GitHub and may be installed via the devtools package by:
devtools::install_github("statnet/EpiModel")
The software source code is available at the Github Repository. Users should submit bug reports and feature requests as issues there.
Documentation
Software Documentation
EpiModel Manual: a PDF manual of the help documentation within the package, with entries for the core package functions.
EpiModel News: major changes were implemented in EpiModel v1.0. This news file (also contained within the package) lists recent software updates.
Main Tutorial
The EpiModel Tutorial provides an overview of the functionality of EpiModel, with a focus on using the integrated model types to parameterize and simulate deterministic and stochastic epidemic models.
EpiModel Web
For beginning EpiModel users and those new to mathematical modeling generally, EpiModel includes two web-based applications for simulating epidemics, using the Shiny framework in R. These applications are included within EpiModel for deterministic compartmental models (DCMs) and stochastic individual contact models (ICMs). They are also hosted online
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Your turn

- **What important questions do you think could be answered with a locally-tuned model?**

- **What would you want to see in such a model?**

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