

Agent-Based Models with an Application to AIDS Research

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Goals today

- ▶ What is agent-based modeling?
- ▶ Applications in social science
- ▶ Application to HIV epidemiology
- ▶ Feel free to interrupt and ask questions!

Agent Based Models

- ▶ Agent-based model is a *'thinking tool'*
- ▶ Agent-based model (ABM) is a computational model used to simulate actions and interactions of autonomous agents
- ▶ Applications in social science are abundant, because social sciences seek to understand how individuals behave and how the interactions lead to large-scale outcomes
- ▶ ABM is well suited for this social science objective

Why model (systems)?

- ▶ In many domains making effective decisions is hard because the system involved exhibits dynamic complexity
- ▶ Failure to understand how a complex system reacts can yield adverse outcomes
- ▶ Reliably anticipating system behavior requires understanding "how it works"
- ▶ Models help hypothesize how a system will behave in counter-factual situations (system vulnerabilities, leverage points, etc.)

Why model (systems)?

- ▶ A few of many uses, serve as "What if" tool to identify desirable policies (cost-effective, high-leverage, robust)
- ▶ Understand benefits of restructuring system
- ▶ Understand trends and help make sense of interaction of diverse information, processes
- ▶ Prioritize research/data collection and identify inconsistencies
- ▶ Understand classes of contexts in which certain strategies are best applied

Complex systems challenges

- ▶ Counter-intuitive behavior
- ▶ Misperceptions
- ▶ Policy resistance
- ▶ Disproportionate impact
- ▶ These phenomena pose problems for:
 - ▶ Learning from experience
 - ▶ Coordinating
 - ▶ Planning and deciding
 - ▶ Designing the system

Issues with traditional approaches and techniques

- ▶ Tightly interrelated and causally tangled pieces
- ▶ Multi-level and multi-pathway (health eco)systems
- ▶ Reciprocal causality
- ▶ Disequilibria
- ▶ Adaptation and learning
- ▶ Significant potential for behavioral and norm shifts
- ▶ Network as cause and effect

Why agent-based models?

- ▶ A common theme: the behavior of the whole is greater than the sum of its parts
- ▶ Decisions based on narrow understanding can lead to "blow-back"
- ▶ Anticipating emergence is required to enact robust and cost-effective interventions, or to avoid doing harm

Why ABMs?

- ▶ Complexity analysis (or systems science) can help us visualize, understand, and reason about implications of underlying (complex) processes
- ▶ A central way of aiding this understanding is via agent-based models
- ▶ ABMs weave together representations of our hypotheses concerning how diverse factors might interact
- ▶ ABMs serve as laboratories for refining our thinking

Brief history

- ▶ ABM didn't really 'take off' until the 1970s (computer use)
- ▶ Cellular automata
- ▶ John Conway's Game of Life (1970): zero-player, two-dimensional game
- ▶ Thomas Schelling's segregation model (1971)

Basic features of agent-based models

- ▶ Model depicts behavior of system over time
 - ▶ Evolving state: Current situation changes over time
 - ▶ The models specify incremental changes (or rate of changes) given current state
 - ▶ System behavior is emergent
 - ▶ Form of model behavior over time cannot be pre-specified in "closed form"
- ▶ Because underlying systems exhibit non-linear characteristics, models generally do as well

Basic features of agent-based models

- ▶ Lack closed-form specification of behavior over time
- ▶ Counter-intuitive behavior
- ▶ Response to multiple interventions very different than sum of responses to each intervention in isolation
- ▶ History (path) dependence
- ▶ Lock-in and multiple possible outcomes
- ▶ Lock-in and multiple possible outcomes
- ▶ Disproportionate pronounced impact of certain groups

(Common) Concern about model scope

- ▶ What quantities are generated by the model (endogenous)?
- ▶ What quantities are represented in the model in a pre-specified way (exogenous)?
- ▶ What quantities are consciously omitted from the model (ignored)?
- ▶ Capturing more factors endogenously adds flexibility, investigative power, accuracy but is also more challenging

Building agent-based model

- ▶ One or more populations composed of individual agent each associated with:
 - ▶ Parameters - discrete (*e.g.* gender, ethnicity) or continuous (*e.g.* birth-weight, income)
 - ▶ State (continuous or discrete) *e.g.* age, smoking status, networks, preferences
 - ▶ Rules for evolving state
 - ▶ Means of interaction with other agents via one or more environments *e.g.* spatial and topological context

Building ABM

- ▶ Time horizon and characteristics
- ▶ Initial state
- ▶ Model Population:
 - ▶ Specify personhood
 - ▶ During simulation each agent has some representation of personhood (sex, income, etc.)
- ▶ Aggregate and spatial emergence, not just eye-candy

Stochastics

- ▶ In contrast to most system dynamics models ABMs are typically stochastic
- ▶ To ensure model results are not merely flukes a model must be run many (many, many) times
 - ▶ this adds to the cost associated to the model
 - ▶ this is easily parallelizable!
- ▶ Stochastics as assets: observing variability can lend insights into the variability of the real-world

Building ABMs

- ▶ It is straightforward to build ABMs featuring multiple levels of context
- ▶ Emergent behavior frequently differs strikingly over different scales

ABM Strengths

- ▶ Capture continuous and discrete heterogeneity
 - ▶ Targeted interventions
 - ▶ Transfer effects (vs. Implicit value judgements)
- ▶ Representing network, spatial context, multi-level nesting
- ▶ Capturing situated decision making, learning (cognitive)
- ▶ Longitudinal info: intervention, calibration

ABM Strengths cont.

- ▶ More precise, endogenous characterization of intervention effects, implementation
- ▶ Visualization aids communication and intuition
- ▶ Synthetic ground truth: capacity for *in silico* assessment of measures and study designs

Some ABM Sources

- ▶ Epstein, Joshua M. and Robert Axtell (1996) "Growing Artificial Societies: Social Science From The Bottom Up"
- ▶ Epstein, Joshua M. (2007) "Generative Social Science: Studies in Agent-Based Computational Modeling"
- ▶ John H. Miller and Scott E. Page (2007) "Complex Adaptive Systems: An Introduction to Computational Models of Social Life"

Application to HIV epidemiology: Motivation

- ▶ Sub-Saharan Africa has the highest Human Immunodeficiency Virus (HIV) prevalence rate in the world
- ▶ Heterosexual transmission of HIV is the leading cause of new HIV infections among adults
- ▶ Randomized trials are assessing the impact of changing various factors leading to infection
- ▶ Simulations can provide insight on key features of HIV transmission and treatment effectiveness within a population
- ▶ So far there has been little success in replicating trajectory of the HIV epidemic in sub-Saharan Africa

Motivation

- ▶ There is no cure for HIV but treatment options exist
- ▶ Antiretroviral Therapy (ART) used for HIV treatment and Pre-Exposure Prophylaxis (PrEP) used for prevention
- ▶ Treatment must be taken for life and is costly (in the US)
- ▶ Guiding research question: at what cost can ART or PrEP be used to drive HIV prevalence in sub-Saharan Africa toward zero?
- ▶ To answer:
 - ▶ Use agent-based model (ABM) and simulate HIV epidemic trajectory
 - ▶ Calibrate models so as to help inform health policy makers in sub-Saharan Africa

Epidemiology of HIV in Sub-Saharan Africa

- ▶ HIV is transmitted through blood, semen, or breast milk from infected person, sexual intercourse, or through infected syringes, and via mother-to-child transfer during pregnancy and birth
- ▶ The leading cause of HIV in Sub-Saharan Africa is heterosexual transmission
- ▶ Focus of research has been on examining aspects of sexual behavior on HIV transmission
- ▶ Three main models to examine: Morris and Kretzschmar (1997), Eaton, Hallett, and Garnett (2011), and Sawers, Isaac, Stillwaggon (2011)

Extending ABM of HIV Spread With Core Groups

MK Model

- ▶ Concurrency can be simply defined at the individual level, but in a population it is more difficult
- ▶ MK use network analysis to define a concurrency measure
- ▶ MK concurrency measure is taken to be the mean degree of the line graph, where line graph represents a partnership
- ▶ Algorithm for producing the network: pair formation, pair dissolution, and disease transmission
- ▶ Pair formation and dissolution are done with a discrete-time Markov model
- ▶ New partnerships form at rate ρ , which depends on the number of present partnerships and they dissolve at a constant rate σ

Extending ABM of HIV Spread With Core Groups

MK Simulation

- ▶ MK run each simulation 100 times (same parameters) for 5 years
- ▶ Use 10 different scenarios of increasing concurrency
- ▶ Average partnership lasts for 6.5 months (mean) and each individual has average 1.22 new sexual partners per year
- ▶ $\rho=0.01$ per day and $\sigma=0.005$ per day; average of 666 partnerships in the population
- ▶ Disease starts by infecting a randomly selected person out of 2000 total (0.05% seed)
- ▶ Disease transmission is a constant daily rate 0.05

Extending ABM of HIV Spread With Core Groups

MK Simulation and Results

- ▶ Results show that epidemic grows faster with increasing concurrency rate
- ▶ For each 10% increase in the average number of concurrent partnerships the final epidemic size rises by roughly 40%
- ▶ MK show that concurrency has an important impact on the early course of an epidemic leading to the exponential growth rate in the number of infected agents
- ▶ Criticism of the model is unrealistically high transmission rate and rapid partner turnover

Extending ABM of HIV Spread With Core Groups

EHG Model and Extensions

- ▶ EHG modify MK model by changing the transmission rate, increasing the seeding prevalence, simulating for 250 years
- ▶ Same as MK, partner selection depends only on presence of primary partner and there is no individual heterogeneity in the propensity to form sexual partnership
- ▶ Concurrency measure: same as MK (11 different levels)
- ▶ Transmission rate: not daily constant rate, rather it varies for different stages of infection

Extending ABM of HIV Spread With Core Groups

EHG Model and Extensions

- ▶ EHG model three different stages of HIV infection: primary (2.9 months), asymptomatic (8.38 years), and symptomatic (9.0 months)
- ▶ Each stage of infection has a daily disease transmission rate associated with it + a period of 10 months with transmission rate = 0
- ▶ Transmission probability:
 - ▶ during primary infection: 0.00732/day
 - ▶ during asymptomatic infection 0.00029/day
 - ▶ during symptomatic infection 0.00208//day
 - ▶ during severe AIDS infection 0.0/day

Extending ABM of HIV Spread With Core Groups

EHG Model Cont.

- ▶ Population is set to 20,000 men and women
- ▶ Epidemic is seeded with randomly infecting 1% of the population with HIV
- ▶ Simulations run for 250 years after the epidemic begins

EHG Model Results.

- ▶ EHG find that increasing concurrency increases prevalence of HIV, however the influence is weaker when transmission probability is constant
- ▶ This model fails to produce the MK type HIV spread (with staged transmission rates) and up to 8% population in concurrent partnership
- ▶ Primary infection substantially increases the role of concurrent sexual partnership
- ▶ EHG model produces HIV epidemics that grow slower than those observed in southern Africa
- ▶ Small groups with greater number of sexual partners and cofactors that increase HIV transmission (and accelerate HIV spread) should be considered

Extending ABM of HIV Spread With Core Groups

SIS Model and Extensions.

- ▶ Sawers, Isaac, and Stillwaggon (SIS) use EHG model and add coital dilution
- ▶ Coital dilution is reduction in per-partner coital frequency with additional partner
- ▶ EHG did not differentiate in coital frequency of primary vs concurrent partnership
- ▶ SIS add lower coital frequencies for all non-primary partnerships
- ▶ Primary simulation assumes 75% coital dilution
- ▶ Same simulation: population 20,000; 11 concurrency levels, simulated over 250 years

Extending ABM of HIV Spread With Core Groups

SIS Model Results

- ▶ At 75% level of coital dilution HIV epidemics is extinct at all levels of concurrency
- ▶ With 75 and 55% coital dilution HIV epidemic is extinct more rapidly at higher levels of concurrency than at lower levels
- ▶ At 25% coital dilution the epidemic spreads at the highest level of concurrency, otherwise it gets extinct
- ▶ Authors conclude that concurrency cannot explain the HIV hyper-epidemic and research should look for other drivers

Extending ABM of HIV Spread With Core Groups

Extensions to MK and EHG Models

- ▶ Address EHG conclusion that small groups with greater number of partners are an important contributor to accelerating the spread of HIV
- ▶ Address mean partnership duration critique of MK and SIS models
- ▶ Add commercial sex workers (CSWs) and mining sector workers to the model
- ▶ These populations have greater number of partners and are at high risk of acquiring and spreading the virus

Extending ABM of HIV Spread With Core Groups

Extensions to MK and EHG Models

- ▶ Some agents will have no resistance to concurrency:
Commercial Sex Workers
- ▶ Some agents will have longer mean primary partnership duration: Mine workers
- ▶ The rest of the population will be parameterized as before
- ▶ Network dynamics and disease transmission will evolve as in MK and EHG models

Extending ABM of HIV Spread With Core Groups

Extensions to MK and EHG Models

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Extending ABM of HIV Spread With Core Groups

Model Setup

- ▶ Generate population (20,000 agents)
- ▶ Randomly infect 1% of the population with the HIV virus
- ▶ Assign given proportion of females CSW attribute and males CSW client attribute
- ▶ Assign given proportion of males MINER attribute
- ▶ Each agent will form (heterosexual) partnership with probability $\rho=0.01$
- ▶ Mean partnership duration will vary; partnership dissolution probability is $\sigma=0.005$ per day
- ▶ During each partnership transmission probability will vary as in EHG; staged transmission
- ▶ Transmit disease if scheduled
- ▶ Dissolve partnership

Extending ABM of HIV Spread With Core Groups Simulations

- ▶ For each value of concurrency (increasing 11 times as MK) simulations are run 100 times
- ▶ Simulations run for 250 years
- ▶ For each year mean HIV prevalence rate is reported
- ▶ Simulations will run for three different proportions of CSW attribute: low, medium, and high
- ▶ Simulations will run one mine worker attribute
- ▶ Sensitivity analysis of relevant parameters

Extending ABM HIV Spread With ART and PrEP Provision

- ▶ There is no cure for HIV but two treatment options exist
- ▶ ABM allows for impact evaluation of adjusting multiple "interventions" treatments at once
- ▶ There are very few efforts to incorporate both treatments into a single model
- ▶ Building on the model of human behavior and HIV spread and adding treatment to HIV dynamics
- ▶ The goal is to identify the best combination of two available treatments that would lead to wiping out the HIV epidemic

Extending ABM of HIV Spread With ART and PrEP Provision

Literature review: ART use

- ▶ Antiretroviral Therapy (ART) has been FDA approved in the US in 1996
- ▶ ART is a combination of several antiretroviral drugs used for HIV treatment
- ▶ ART lead to decline in morbidity and mortality due to HIV
- ▶ Models examining potential impact of ART intervention are hard to quantify and results vary greatly
- ▶ How much will use of ART reduce HIV prevalence is an empirical issue
- ▶ Research examining (potential) impact of ART can be divided into empirical studies and mathematical models

Literature on ART use

- ▶ Empirical studies on impact of ART find:
 - ▶ ART reduces the viral load in the infected person (Cohen and Gay 2010, Melo et al. 2008, etc.)
 - ▶ ART use reduces the HIV prevalence among non-infected partners (Melo et al. 2010)
- ▶ ART use has contributed to decline in morbidity and mortality due to HIV (WHO)
- ▶ Cohen et al. (2010) report 96% reduction in HIV transmission with ART use
- ▶ Mathematical models examining potential impact of ART focus on cost-effectiveness. Less relevant with advent of PrEP.

Literature on PrEP use

- ▶ PrEP treatment (drug called Truvada) approved in the US in 2012
- ▶ It is a type of ART taken by the HIV-negative individuals to reduce their individual risk of acquiring HIV
- ▶ Truvada is expensive: about \$1500 a month (in the US)
- ▶ Research on PrEP cost-effectiveness is quickly growing
- ▶ Research on budgetary consequences of trying to add PrEP to existing ART programmes is not

Literature on PrEP use

- ▶ Key models to consider are mathematical models of cost-effectiveness of PrEP and ART, modeling drug adherence and resistance, with focus on heterosexual couples (Hallet et al (2011), Long and Stavert (2013), and Nichols et al. (2013))
- ▶ Comparison is difficult: different levels of model complexity, different assumption dependence, inherent model uncertainty
- ▶ Consensus is that ART and PrEP are cost effective and lead to gains in quality adjusted life years (QALY) in any scenario

Model Setup

- ▶ Utilizing data and parameter values from mathematical models and empirical findings build upon ABM with CSWs and miners
- ▶ Model set up as before: 20,000 agents, 250 years, allowing for 11 levels of concurrency, dilution, two core groups and two treatments
- ▶ Assumption about ART:
 - ▶ lowers transmission by 96% in all stages of infection
 - ▶ availability can be low or high (sensitivity analysis)
- ▶ Assumptions about PrEP:
 - ▶ availability can be low or high (sensitivity analysis)

- ▶ Parameterization without proper data
- ▶ Lack of transmission rates in different stages of HIV infection
- ▶ Model set up (initialization)
- ▶ Treatment adherence

ABM Calibration/Future Work

- ▶ Model validation is done using:
 - ▶ matching model components and processes to real-world components and processes, and
 - ▶ matching both simulated patterns to real-world patterns and comparing quantitative model output with measured variables (Bert et al., 2014).

- ▶

ABM Calibration

Case Study: Botswana, Zambia, South Africa

- ▶ Botswana, Zambia, and South Africa are all resource rich
- ▶ All three exhibit a different HIV profile/trajectory of virus spread
- ▶ Botswana is rich in diamonds, South Africa in diamonds and gold, Zambia in copper
- ▶ Botswana has the highest HIV prevalence rate, followed by South Africa, and Zambia (UNAIDS, 2013)

Future work

Case Study: Botswana, Zambia, South Africa

- ▶ Proper calibration will depend on data availability
- ▶ Ideally model calibration and validation would incorporate Geographic Information System (GIS) spatial data

- ▶ Questions?
- ▶ Thank you!