



Review

A New Tool for Epidemiology: The Usefulness of Dynamic-Agent Models in Understanding Place Effects on Health

Amy H. Auchincloss and Ana V. Diez Roux

From the Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, MI.

Received for publication September 25, 2007; accepted for publication January 29, 2008.

A major focus of recent work on the spatial patterning of health has been the study of how features of residential environments or neighborhoods may affect health. Place effects on health emerge from complex interdependent processes in which individuals interact with each other and their environment and in which both individuals and environments adapt and change over time. Traditional epidemiologic study designs and statistical regression approaches are unable to examine these dynamic processes. These limitations have constrained the types of questions asked, the answers received, and the hypotheses and theoretical explanations that are developed. Agent-based models and other systems-dynamics models may help to address some of these challenges. Agent-based models are computer representations of systems consisting of heterogeneous microentities that can interact and change/adapt over time in response to other agents and features of the environment. Using these models, one can observe how macroscale dynamics emerge from microscale interactions and adaptations. A number of challenges and limitations exist for agent-based modeling. Nevertheless, use of these dynamic models may complement traditional epidemiologic analyses and yield additional insights into the processes involved and the interventions that may be most useful.

computer simulation; environment and public health; epidemiologic methods; health behavior; models, theoretical; residence characteristics; systems theory

Editor's note: An invited commentary on this article appears on page 9.

As a component of the epidemiologic triad of person, place, and time, place-related factors have long been thought to provide important clues on the causes of ill health. A major focus of recent work in epidemiology has been the study of how features of residential environments or neighborhoods may affect health. The identification of causal effects of neighborhoods on health would have important policy implications, as it would illustrate the possible health impact of policies regarding urban planning, transportation, and community development.

Recent reviews of work on neighborhood health effects have focused mostly on methodological challenges related

to the use of statistical models to estimate causal neighborhood effects from observational data—particularly on measurement of area-level variables, definition of the relevant spatial scale, and the problem of nonexchangeability of persons living in different neighborhoods (1–4). In this paper, we discuss a distinct set of challenges derived from the fact that the spatial patterning of health emerges from the functioning of a system in which individuals interact with each other and their environment and in which both individuals and environments adapt and change over time. We propose adding a new methodology, *agent-based models*, which may help to address these challenges, and we discuss fundamental issues in the implementation of this approach. Although we use the study of neighborhood effects on health behaviors as a motivating example, many of the issues that we discuss are relevant to other research questions in both social epidemiology and epidemiology more generally.

SELECTED CHALLENGES FOR STUDYING THE EFFECTS OF PLACE ON HEALTH

The conceptual challenge, the interrelatedness of persons and environments

The neighborhood patterning of health behaviors results from a web of conditions and feedback loops including the multiple related processes listed in table 1. Persons are sorted (or selected) into neighborhoods on the basis of external constraints related to socioeconomic resources and discrimination (resulting in residential segregation by class and race), as well as preferences for neighborhoods with particular features. These selection processes lead to spatial clustering by individual-level attributes (e.g., income) that are related to health behaviors. Health behaviors are also affected by residential environments, such as whether the environment has recreational resources and places to purchase healthy foods. Norms may emerge in the context of places as a result of the predominant health behaviors in the area, and individual health behaviors may in turn change in response to these norms. Neighborhoods also change in response to residents' characteristics and preferences and in response to the features of surrounding or related neighborhoods. Specific examples of each of these processes applied to place influences on physical activity are provided in table 1. The spatial patterning of health behaviors emerges from the simultaneous operation of all these processes, making it challenging to empirically isolate one from the other.

The methodological challenge, the limits of regression

Multilevel analysis has been the main analytical approach used in recent years to identify causal effects of places on health (5–7). The main motivation for the use of multilevel analysis has been the desire to estimate effects of place-related characteristics on individual-level health outcomes after statistical controls for individual-level attributes believed to be simultaneously related to both health and spatial location. By summarizing regularities in the data and estimating “independent” associations of place factors with individual-level outcomes, multilevel analysis has been used to test hypotheses regarding the presence of place effects. However, like other regression-based approaches, these models necessarily simplify complex interrelations. For example, in most applications, multilevel analyses address only the first two processes listed in table 1. Although multilevel models can sometimes be adapted to allow for some of the other processes listed, the focus on decomposition of variability and estimating “independent” effects necessarily isolates elements from each other and ignores feedback loops. A number of other methodologies have been utilized within a very restricted framework to address the shortcomings of traditional regression-based approaches, such as accounting for the confounding effects of the variables affected by prior treatment (e.g., marginal structural models (8)) or examining a very limited set of feedback mechanisms (e.g., loop analyses (9)). However, in general, regression approaches continue to be ill equipped to investigate the processes embedded in complex systems characterized by

TABLE 1. Selected processes generating place differences in health behaviors and examples from the study of neighborhood patterning of physical activity

| Processes generating place differences in health behaviors | Example for being physically active |
|-------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1. Person-level health is affected by features of the residential neighborhood. | The availability of places to be physically active promotes physical activity. |
| 2. Persons are selected into residential neighborhoods on the basis of their person/household-level attributes. | Individuals are sorted into neighborhoods that are affordable to them (income) and welcoming of them (age and race/ethnicity). These characteristics are potentially related to being physically active. |
| 3. Persons select their residence on the basis of their preferences for features of residential neighborhoods. | Neighborhoods that have safe and aesthetically pleasing places to be physically active attract persons who prefer to be physically active. |
| 4. Persons adapt their behaviors in response to collective behaviors within their spatial (and social) network and wider geographic area. | Seeing more bicycle riders may increase the likelihood of commuting to work via bike. |
| 5. Neighborhoods adapt in response to residents' characteristics. | Gyms and places to engage in sports are more likely to locate in areas where individuals are known to be physically active, in wealthier areas where individuals have greater purchasing power, or in areas where physically active residents advocate for them. |
| 6. Neighborhoods adapt in response to features of other neighborhoods or more distant places. | Regional transport infrastructure affects the availability of public transportation and automobile restrictions in local neighborhoods. |

dynamic interactions between heterogeneous individuals and interactions between individuals and their environment with multiple feedback loops and adaptation.

The data challenge, the limits of available data and study designs

Because regression-based approaches such as multilevel analysis are used to draw conclusions regarding causal associations on the basis of empirical regularities in data, their validity is closely tied to the data available. Moreover, the vast majority of analyses of place effects on health are based on observational data with well-known limitations for causal inference (10). These limitations have led some researchers to call for increasing the use of randomized trials in the study of the effects of residential environments on health (2). Experimental studies in which persons/households are randomized into different environments or in which places are randomized into environmental interventions may be unethical or logistically infeasible (3).

Moreover, experimental approaches (or their observational approximations) attempt to isolate the effect of changing a single factor while holding all the other features of the system constant. However, in the context of dynamic interactions and feedback loops, the effects of changing a single factor may be contingent on features of the system and, thus, may not be generalizable. Identifying the circumstances under which they may or may not be generalizable requires moving beyond the “black box approach” and understanding the processes involved. Experiments and their observational approximations yield few insights into these processes particularly when they involve feedback loops and adaptation, yet understanding these processes may be important for predicting the effects of the intervention under other scenarios and for identifying alternate interventions that may achieve the desired effect.

AGENT-BASED MODELS AS A COMPLEMENT TO EXISTING APPROACHES

Agent-based models have been increasingly adopted in the social and geographic sciences to investigate processes involving interactions between heterogeneous units and dynamic interactions between units and environments, including processes leading to the spatial patterning of a variety of individual-level outcomes (11, 12). We discuss what defines agent-based modeling, why these models may be advantageous in understanding place effects on health, and an example of the use of agent-based models to study the processes generating neighborhood differences in health behaviors. We also discuss limitations and challenges in this new approach.

What is an agent-based model?

Agent-based models are computer representations of systems consisting of a collection of discrete microentities interacting and changing over discrete time steps that give rise to macrosystems (13–16). The microentities, referred to as “agents,” are anything that alters its behavior in response to input from other agents and the environment (17). In models investigating how residential environments may impact physical activity, we can include highly diverse agents that respond to or alter environments for physical activity, such as individuals, recreation facilities, schools, and city-planning entities. Agents are given traits and initial behavior rules that organize their actions and interactions (16, 18). Stochasticity can be included in the assignment of agent characteristics and in determining which agents interact and how agents obtain information and make decisions (19). The model is run over time and repeated numerous times to obtain a distribution of possible outcomes for the specified system.

Example using agent-based models to investigate determinants of the spatial patterning of physical activity

We illustrate an abstract agent-based model that could be used to examine processes (listed in table 1) that contribute

to the spatial patterning of leisure-time physical activity among working-age women. We start with two types of agents, individuals and recreation facilities, and situate them within an urban environment. Agents are assigned a few characteristics relevant to the process being studied. For this model, women are given a physical activity level (all begin at the same level), income, and quantity of leisure time. Recreational facilities are characterized as free or charging a fee for use. Agents are given behaviors that initially are quite simple but can be made more complex. For example, the women prefer to be physically active, but their ability to meet this goal is constrained by wanting to minimize the time spent exercising (including the time spent travelling to a facility) and the financial cost of exercising. These behaviors are dependent on the person’s available leisure time and income (i.e., the more time and money she has, the more likely she is to use more time and money). Recreational facilities have a goal of maximizing the number of women that use their facility and will decide where to locate on the basis of facility attendance and the number of recreational resources in the area. Parameter values and decision rules/algorithms for behaviors must have some (even loose) empiric foundation (14). Income-level distributions can come from census data, initial physical activity levels and preference parameterization can come from physical activity surveys (20–25), and leisure time and additional information on physical activity participation can come from time use surveys (26). Recreational facility parameterization and rules can be derived from data on commercial citing and pricing (27) and from prevalence, utilization, and geographic spacing of recreational facilities (28–31). Common elements across data sets (e.g., age) can be used to derive a plausible range of joint distributions with which to parameterize the model. Uncertainty and randomness in decision making can be incorporated by drawing parameters from a statistical distribution and including stochastic processes.

Just as regression models are often refined by progressively adding elements to identify the drivers of effects, agent-based models often begin with a very simple model of core elements that is then progressively rendered more complex by adding more elements. It would be wise to initially model only processes 1, 2, and 5 from table 1. Subsequent models would progressively add more complexity, such as networking individuals into a spatial proximity/small-world network (32) using prior research regarding network influence on behaviors (33, 34). Agent-based models are programmed in object-oriented languages (e.g., Java (Sun Microsystems, Santa Clara, California) and C++ (Bell Laboratories, Murray Hill, New Jersey)) that can manipulate heterogeneous agent types, behaviors, and dynamic interrelations. Swarm (35), MASON (36), RePast (37), and NetLogo (38) are examples of software used for agent-based models.

Like many agent-based models, the model illustrated above can be used for two purposes. One purpose is to extend theory and to test hypotheses about fundamental processes (39) involved in the ways that the spatial distribution of resources relates to the spatial distribution of physical activity. For example, various starting conditions regarding the spatial location of recreational facilities could be used to explore how differences in the spatial location of facilities

contribute to neighborhood differences in physical activity. Because of their abstract nature, these types of models have been referred to as “theoretical experimentation” (40) or “thought experiments” (41). Conceptually, thought experiments (41) in agent-based models have similarities to testing “what if” artificial counterfactual conditions in causal modeling (42). A key difference, however, is that in agent-based models these counterfactual comparisons take place in the context of explicitly modeled dynamic and reciprocal relations. This allows for much more nuanced conclusions regarding the circumstances under which a given intervention or change does or does not produce a given effect.

A second purpose of this model could be prognostic (19). The model could be used to assess whether certain interventions can alter physical activity levels among residents and thereby influence the spatial patterning of physical activity or reduce social inequalities in physical activity. Examples of possible interventions are as follows: making recreational facilities more attractive (e.g., improvements to the quality or safety of urban parks), promoting the placement of facilities in underserved areas, or reducing the cost of gym facilities in poor areas (43). Because of the stochastic nature of microprocesses, agent-based models are not well suited for detailed predictions, but they can be used to examine the range of system effects an intervention or change in policy might be expected to have (19, 44, 45).

Other agent-based models that have been used to study spatial patterning

Although agent-based models have rarely been used in epidemiology (46–48), they are increasingly used in a wide variety of disciplines to model dynamic heterogeneous behaviors (49–51). We will briefly mention a few examples of work that used agent-based models to investigate processes similar to those listed in table 1. One now classic example is Schelling’s abstract agent-based model of racial residential segregation (52), which showed that, even when the majority of residents do not prefer to live in segregated neighborhoods, their aversion preferences (not wanting to be a “minority” in their neighborhood) dominate interactions and result in highly segregated neighborhoods. His model was very simple, yet it highlighted how spatial patterning (in this case spatial patterning of race) can emerge from micro-level interactions in ways that cannot be predicted easily with traditional approaches. Another example of how agent-based models have been used to study spatial patterning is urban sprawl models developed by urban planners and geographers (11, 12). Brown and Robinson (11) and Brown et al. (50) have shown how large-scale residential movement away from urban centers can occur as households respond to features of neighborhoods (e.g., availability of jobs and urban service centers) and weigh multiple and conflicting residential preferences (e.g., desire to live in an attractive area but be close to jobs). Ultimately, these models have been used to obtain insight into whether urban land use policies could alter urban sprawl. Eubank et al. (47) and Barrett et al. (53) have used agent-based models to study the impact of spatially constrained social networks on the dispersion of smallpox. They constructed a social/geographic contact net-

work based on a highly detailed urban transportation grid in actual cities (i.e., Houston, Texas, and Portland, Oregon), census data, and surveys of time-activity patterns. Ultimately, these models were used to make recommendations regarding the timing and location for smallpox vaccination if an outbreak were to occur under various scenarios.

ADVANTAGES OF AGENT-BASED MODELS IN STUDYING THE EFFECTS OF PLACE ON HEALTH

Conceptual utility of agent-based models

Conceptually, agent-based models have several attractive features for investigating questions related to the spatial patterning of health. They explicitly allow for dynamic interactions between heterogeneous individuals and between individuals and environments. Although agent-based models are a “bottom-up” approach (13) in that macroscale dynamics emerge from microscale agent interactions and adaptations, they also provide a theoretical bridge between the macro- and microlevels (54), because feedback connects the two levels such that macroproperties emerge from micro-level interactions that in turn influence microlevel behaviors. In addition, agent-based models allow for agents defined at multiple levels, including levels above individuals (e.g., recreational facilities, policy-making bodies, etc.).

Methodological utility of agent-based models

The key methodological advantage of agent-based models is that they can be used to model the dynamic processes related to place effects on health. In contrast to regression approaches that summarize empirical regularities to learn about causal processes from this description, agent-based models model the specific processes believed to give rise to the empirical regularities observed (15, 55). This focuses attention on interdependent processes rather than just “independent” associations between variables. For example, the traditional regression approach would attempt to estimate the independent association between recreational resource availability and physical activity after statistical controls for other area-level or individual-level factors. In contrast, the agent-based model approach would attempt to model the ways in which persons interact with each other and their environments and change and adapt in response to these interactions; it would also attempt to model the ways in which the environment changes in response to the actions of individuals. Rather than ignoring these feedback and adaptation processes (which generate endogeneity (56)), agent-based models explicitly model the sources of this endogeneity and allow examination of how these feedback and adaptation processes contribute to the patterns observed.

Data utility of agent-based models

Agent-based models do not resolve the difficulties in obtaining empirical data relevant to investigating the effects of place on health. However, the development of these models

(which requires information on empirical relations in order to specify realistic parameters and algorithms) will often acutely highlight areas for which empirical data are lacking (57). For example, in developing an agent-based model of neighborhoods and physical activity, it may become apparent that we have little empirical information on how cost and distance affect the utilization of recreational resources for different demographic groups. This would promote additional data collection on this question. In addition, agent-based models actually generate longitudinal data for an artificial society (13) and, therefore, allow evaluation of hypothetical interventions, an exercise that would be impossible to do by collecting and analyzing real-world data.

CHALLENGES FOR AGENT-BASED MODELS

Distill complex worlds into relatively simple dynamics

As with all models, a tension exists in agent-based models to make them both simple enough to yield useful insights and complex enough not to misrepresent what is going on in the real world (16). Many modelers argue that the most interesting analytical results are obtained when complexity at the macrolevel is produced by simple microlevel dynamics. Robert Axelrod's keep-it-simple-and-stupid principle (58), often referred to as "KISS," codified this position.

There is a practical reason for this: Very complicated models with high levels of agent diversity, interactions, and adaptation/learning can potentially have too many dynamic processes and too many outcomes (16, 57). Incorporating so many moving parts, models become impossibly difficult to interpret and validate. There is also a substantive reason: Agent-based models are discrete-event simulations (19), yet they are distinct from traditional simulations that tend to try to accurately represent a specific empirical situation or exact details of a specific empirical problem. Rather, agent-based models tend to try to understand fundamental processes that may appear in a variety of applications (55).

There is no formula for what to include in an agent-based model. Nevertheless, it is widely recommended that 1) the question be quite simple but involve complex processes; 2) the model focus on the most critical elements of the processes of interest; 3) higher levels of diversity and interactions be added in steps; and 4) submodels be nested within the larger model. Place effects on health involve a complicated process, yet questions can be constrained; for example, does spatial patterning of leisure-time physical activity resources influence physical activity among working-age women? Given a very specific question, it is possible to identify a limited number of agents, environmental features, and interactions in order to examine this question.

Model validity and transparency

The relevance of the results of agent-based models to questions that relate to place effects on health will depend on the adequacy with which the model captures the fundamental processes operating in reality. One way to ensure a reasonable linkage to reality is to base parameter values and decision rules/algorithms for behaviors on empirical

data. It can be a challenge to locate detailed relevant data with which to parameterize a model. A solution to this challenge is to use a variety of data sources (e.g., census data, behavioral research, time activity data) and, when there is only weak justification for particular parameterizations, exploratory models can be used to examine the sensitivity of results to varying specifications.

Given that agent-based models can reveal counterintuitive processes, evaluating agent-based model validity can be a challenge. Unexpected results may be due to errors in computer programming, path-like dependencies (when the system's outcome is highly dependent on initial choices or small variations in stochastic processes due to strong positive feedback), or truly surprising but truthful and informative properties. Approaches to addressing these challenges are robustness testing and "docking" models to other models (59). Robustness testing in agent-based models involves running the model multiple times, systematically varying initial conditions or parameters in order to assess the stability of results (60). Robustness testing also involves contrasting the model's macrolevel endpoints (e.g., quasi-steady states) with macrosystems observed in the real world (for more discussion, refer to the chapter by Brown in the book edited by Geist (19) and the article by Rykiel (61)). For example, does our model generate the nonrandom spatial patterns of physical activity similar to those observed in urban areas (30, 31)?

Docking models is the process of aligning multiple models that address similar fundamental concepts. Alignment can be done between different agent-based models (59) or across modeling methodologies. Docking across methodologies is possible if the agent-based model is stripped to the common elements it shares with the other models. For example, in a comparison of an agent-based model with traditional regression, the agent-based model would need to be stripped to a nondynamic model. This type of test can also assess whether dynamic feedbacks and interactions are important drivers of model inference or whether complex dynamics can essentially be ignored in favor of simpler approaches. Given the challenges with model validity, a number of approaches need to be used and, ultimately, selection among competing models that yield similar outputs compatible with real world observations may have to rely on other types of evidence, as well as substantive knowledge brought to bear by the investigator.

A final challenge for research on place effects on health is that the use of agent-based models requires new scientific protocols and language for describing what was done. A solution to this challenge is to follow recently developed standard protocols for conducting and describing agent-based models (14, 62). Following such standards will greatly increase the transparency of models and will provide a language that the scientific community can use to evaluate model validity.

COMBINING AGENT-BASED MODELS WITH OTHER SYSTEMS-MODELING APPROACHES

Agent-based models are only one of several modeling approaches that can be used to investigate systems or

complex systems. Among these, (systems) dynamic equation models have been among the most commonly used in epidemiologic and health services research (63–66). These models use sets of differential equations to model population dynamics as stocks and flows (such as flows of information or risk states) among continuous segments of the population (rather than individuals) (67). Briefly, there are a number of advantages to systems models over agent-based models (68, 69). Compared with agent-based models, large populations can be modeled with relative ease, and systems model outputs tend to be easier to understand and communicate, mainly because of being equation based and thus having familiar mathematical foundations (14). In this paper, we concentrated on agent-based models because of their ability to easily model heterogeneity and diverse spatial elements (70, 71). For example, agent-based models can relatively easily incorporate spatially explicit diverse local networks, behaviors, and interactions, and spatially located environmental resources can move and interact with heterogeneous individuals. Often, it may be useful to combine modeling methodologies (e.g., regression, agent-based models, and dynamic equations). For example, parameter inputs for agent-based models can be derived by use of multilevel regression models; agent-based models can be used to derive realistic flows/rates for dynamic equation models and to identify important sources of heterogeneity that need to be modeled (72); and subsequent dynamic equation models can model aggregate-level processes and develop tractable mathematical predictions. Approaches that combine methodologies or that compare results by use of different methodologies (using the methods described above for docking models) may be useful to examine the place effects on health and interventions or policies to improve health.

CONCLUSION

Just as multilevel analysis promoted thinking about multilevel determinants, agent-based models may promote thinking about the ways individuals interact with each other and with their environments. Too often, the exclusive use of regression approaches constrains not only the answers we get but also the types of questions we pose and the hypotheses and even theoretical explanations that we develop. In our search for what is “tractable” in empirical observational research (essentially that which mimics the perfect experiment), our questions have the tendency to become narrower and narrower and perhaps less relevant to understanding or intervening in the real world (16). By allowing us to explore dynamic, nonlinear, heterogeneous, reciprocal spatio-temporal processes, the agent-based modeling approach can open up our thinking to new conceptualizations of place effects on health. Initially, the use of agent-based models in understanding the spatial patterning of health will have to be exploratory and developmental. A fundamental challenge is to keep models simple, yet sufficiently informative. Another challenge is making abstract agent-based models useful for decision making and policy. Yet, at a minimum, these dynamic models will stimulate creative thinking about the processes involved in place effects on health and expand

the range of questions being asked. Dynamic models not only bring new tools to the research endeavor but also may stimulate us to think more broadly and perhaps more realistically about the complex processes we are trying to investigate. This may allow us to develop more sophisticated theoretical models of the processes involved in the spatial patterning of health, models that we can subsequently test empirically by a variety of approaches, be they experimental, observational, or complex systems modeling.

ACKNOWLEDGMENTS

Funding for this work came from the National Heart, Lung, and Blood Institute (grant R01 HL071759) and the National Institute of Child Health and Human Development (grant 1R24 HD047861).

Conflict of interest: none declared.

REFERENCES

1. Macintyre S, Ellaway A, Cummins S. Place effects on health: how can we conceptualize, operationalize and measure them? *Soc Sci Med* 2002;55:125–39.
2. Oakes JM. The (mis)estimation of neighborhood effects: causal inference for a practicable social epidemiology. *Soc Sci Med* 2004;58:1929–52.
3. Subramanian SV. The relevance of multilevel statistical methods for identifying causal neighborhood effects. *Soc Sci Med* 2004;58:1961–7.
4. Diez Roux AV. Integrating social and biologic factors in health research: a systems view. *Ann Epidemiol* 2007;17:569–74.
5. Duncan C, Jones K, Moon G. Context, composition and heterogeneity: using multilevel models in health research. *Soc Sci Med* 1998;46:97–117.
6. Diez Roux AV. Multilevel analysis in public health research. *Annu Rev Public Health* 2000;21:171–92.
7. Bingenheimer JB, Raudenbush SW. Statistical and substantive inferences in public health: issues in the application of multilevel models. *Annu Rev Public Health* 2004;25:53–77.
8. Hernan MA, Brumback B, Robins JM. Marginal structural models to estimate the causal effect of zidovudine on the survival of HIV-positive men. *Epidemiology* 2000;11:561–70.
9. Dinno A. Loop analysis of causal feedback in epidemiology: an illustration relating to urban neighborhoods and resident depressive experiences. *Soc Sci Med* 2007;65:2043–57.
10. Winship C, Morgan SL. The estimation of causal effects from observational data. *Annu Rev Sociol* 1999;25:659–706.
11. Brown DG, Robinson DT. Effects of heterogeneity in residential preferences on an agent-based model of urban sprawl. (Electronic article). *Ecol Soc* 2006;11:46. (<http://www.ecologyandsociety.org/vol11/iss1/art46/>).
12. Torrens PM. Simulating sprawl. *Ann Assoc Am Geogr* 2006;96:248–75.
13. Epstein JM, Axtell R. *Growing artificial societies: social science from the bottom up*. Washington, DC: Brookings Institution Press, 1996.
14. Grimm V, Railsback SF. *Individual-based modeling and ecology*. Princeton, NJ: Princeton University Press, 2005.
15. Miller JH, Page SE. *Complex adaptive systems*. Princeton, NJ: Princeton University Press, 2007.

16. Page SE. Agent-based models. In: Durlauf SN, Blume LE, eds. *The new Palgrave dictionary of economics*. 2nd ed. New York, NY: Palgrave Macmillan, 2008. (http://www.dictionaryofeconomics.com/article?id=pde2008_A000218&goto=agentbasedmodels&result_number=16).
17. Bonabeau E. Agent-based modeling: methods and techniques for simulating human systems. *Proc Natl Acad Sci U S A* 2002;99:7280–7.
18. Holland JH. *Hidden order: how adaptation builds complexity*. New York, NY: Addison Wesley Publishing Company, 1996.
19. Brown DG. Agent-based models. In: Geist H, ed. *The earth's changing land: an encyclopedia of land-use and land-cover change*. Westport, CT: Greenwood Publishing Group, 2006: 7–13.
20. Evenson KR, Sarmiento OL, Macon ML, et al. Environmental, policy, and cultural factors related to physical activity among Latina immigrants. *Women Health* 2002;36:43–57.
21. Hu G, Sarti C, Jousilahti P, et al. Leisure time, occupational, and commuting physical activity and the risk of stroke. *Stroke* 2005;36:1994–9.
22. Macera CA, Ham SA, Yore MM, et al. Prevalence of physical activity in the United States: Behavioral Risk Factor Surveillance System, 2001. (Electronic article). *Prev Chronic Dis* 2005;2:A17. (http://www.cdc.gov/pcd/issues/2005/apr/04_0114.htm).
23. Azevedo MR, Araujo CL, Reichert FF, et al. Gender differences in leisure-time physical activity. *Int J Public Health* 2007;52:8–15.
24. Jilcott SB, Evenson KR, Laraia BA, et al. Association between physical activity and proximity to physical activity resources among low-income, midlife women. (Electronic article). *Prev Chronic Dis* 2007;4:A04. (<http://www.pubmedcentral.nih.gov/picrender.fcgi?artid=1832127&blobtype=pdf>).
25. Reichert FF, Barros AJ, Domingues MR, et al. The role of perceived personal barriers to engagement in leisure-time physical activity. *Am J Public Health* 2007;97:515–19.
26. Bureau of Labor Statistics. *American Time Use Survey*. Washington, DC: Department of Labor, 2006. (<http://www.bls.gov/tus/home.htm>).
27. Ghosh A, Craig CS. An approach to determining optimal locations for new services. *J Mark Res* 1986;23:354–62.
28. Sallis JF, Hovell MF, Hofstetter CR, et al. Distance between homes and exercise facilities related to frequency of exercise among San Diego residents. *Public Health Rep* 1990;105:179–85.
29. Hoehner CM, Brennan Ramirez LK, Elliott MB, et al. Perceived and objective environmental measures and physical activity among urban adults. *Am J Prev Med* 2005;28:105–16.
30. McCormack GR, Giles-Corti B, Bulsara M, et al. Correlates of distances traveled to use recreational facilities for physical activity behaviors. (Electronic article). *Int J Behav Nutr Phys Act* 2006;3:18. (<http://www.pubmedcentral.nih.gov/picrender.fcgi?artid=1557534&blobtype=pdf>).
31. Diez Roux AV, Evenson KR, McGinn AP, et al. Availability of recreational resources and physical activity in adults. *Am J Public Health* 2007;97:493–9.
32. Watts DJ, Strogatz SH. Collective dynamics of 'small-world' networks. *Nature* 1998;393:440–2.
33. Emmons KM, Barbeau EM, Gutheil C, et al. Social influences, social context, and health behaviors among working-class, multi-ethnic adults. *Health Educ Behav* 2007;34:315–34.
34. Brownson RC, Baker EA, Housemann RA, et al. Environmental and policy determinants of physical activity in the United States. *Am J Public Health* 2001;91:1995–2003.
35. Minar N, Burkhart R, Langton C, et al. The Swarm Simulation System: a toolkit for building multi-agent simulations. Santa Fe, NM: Santa Fe Institute, 1996. (Working paper 96-06-042) (<http://www.swarm.org/wiki/Image:MinarEtA196.pdf>).
36. Luke S, Cioffi-Revilla C, Panait L, et al. MASON: a new multi-agent simulation toolkit. In: *Proceedings of the 2004 SwarmFest Workshop*. Fairfax, VA: Department of Computer Science and Center for Social Complexity, George Mason University, 2004. (<http://www.cs.gmu.edu/~eclab/projects/mason/publications/SwarmFest04.pdf>).
37. Tataru E, North M, Howe T, et al. An introduction to RePast simphony modeling using a simple predator-prey example. In: *The Agent 2006 Conference on Social Agents: Results and Prospects*. Chicago, IL: Argonne National Laboratory and the University of Chicago, 2006. (http://repast.sourceforge.net/papers/Agent_2006_Repast_Tutorial.pdf).
38. Wilensky U. *NetLogo*. Evanston, IL: Center for Connected Learning and Computer-based Modeling, Northwestern University, 1999. (<http://ccl.northwestern.edu/netlogo/>).
39. Parker DC, Hessel A, Davis SC. Complexity, spatial modeling, and the human dimension: fundamental challenges for mapping unknown outcome spaces. *Geoforum special issue, "Biocomplexity in coupled human-natural systems"* (in press).
40. Macy MW, van de Rijt A. Ethnic preferences and residential segregation: theoretical explorations beyond Detroit. *J Math Sociol* 2006;30:275–88.
41. Di Paolo E, Nobe J, Bullock S. Simulation models as opaque thought experiments. Presented at *Artificial Life VII: The Seventh International Conference on the Simulation and Synthesis of Living Systems*, Reed College, Portland, Oregon, August 1–6, 2000.
42. Maldonado G, Greenland S. Estimating causal effects. *Int J Epidemiol* 2002;31:422–9.
43. Jilcott SB, Laraia BA, Evenson KR, et al. A guide for developing intervention tools addressing environmental factors to improve diet and physical activity. *Health Promot Pract* 2007; 8:192–204.
44. Bankes S. Exploratory modeling for policy analysis. *Oper Res* 1993;41:435–49.
45. Bankes SC. Tools and techniques for developing policies for complex and uncertain systems. *Proc Natl Acad Sci U S A* 2002;99:7263–6.
46. Epstein JM, Cummings DAT, Chakravarty S, et al. *Toward a containment strategy for smallpox bioterror: an individual-based computational approach*. Washington, DC: Brookings Institution Press, 2004.
47. Eubank S, Guclu H, Anil Kumar VS, et al. Modelling disease outbreaks in realistic urban social networks. *Nature* 2004;429: 180–4.
48. Gorman DM, Mezić J, Mezić I, et al. Agent-based modeling of drinking behavior: a preliminary model and potential applications to theory and practice. *Am J Public Health* 2006;96: 2055–60.
49. Macy MW, Flache A. Learning dynamics in social dilemmas. *Proc Natl Acad Sci U S A* 2002;99:7229–36.
50. Brown DG, Page S, Riolo R, et al. Agent based and analytical modeling to evaluate the effectiveness of greenbelts. *Environ Model Softw* 2004;19:1097–109.
51. Fowler CS. Taking geographical economics out of equilibrium: implications for theory and policy. *J Econ Geogr* 2007;7:265–84.
52. Schelling TC. *Micromotives and macrobehavior*. New York, NY: WW Norton & Co, Inc, 1978:147–65.
53. Barrett CL, Eubank SG, Smith JP. If smallpox strikes Portland. . . . *Sci Am* 2005;292:42–9.
54. Macy MW, Willer R. From factors to actors: computational sociology and agent-based modeling. *Annu Rev Sociol* 2002; 28:143–66.

55. Axelrod RM. Complexity of cooperation. Princeton, NJ: Princeton University Press, 1997.
56. Manski CF. Identification of endogenous social effects: the reflection problem. *Rev Econ Stud* 1993;60:531–42.
57. Committee on Frontiers at the Interface of Computing and Biology. Computational modeling and simulation as enablers for biological discovery. In: Wooley JC, Lin HS, eds. Catalyzing inquiry at the interface of computing and biology. Washington, DC: Computer Science and Telecommunications Board, Division on Engineering and Physical Sciences, National Research Council of the National Academies, 2005.
58. Axelrod R. Advancing the art of simulation in the social sciences. In: Conte R, Hegselmann R, Terna P, eds. Simulating social phenomena. Berlin, Germany: Springer, 1997:21–40.
59. Axtell R, Axelrod R, Epstein JM, et al. Aligning simulation models: a case study and results. *Comput Math Organ Theory* 1996;1:123–41.
60. Axtell R. Why agents? On the varied motivations for agent computing in the social sciences. Washington, DC: Brookings Institution, 2000. (Center on Social and Economic Dynamics (CSED) working paper 17) (http://www.brookings.edu/reports/2000/11technology_axtell.aspx).
61. Rykiel EJ. Testing ecological models: the meaning of validation. *Ecol Modell* 1996;90:229–44.
62. Grimm V, Berger U, Bastiansen F, et al. A standard protocol for describing individual-based and agent-based models. *Ecol Modell* 2006;198:115–26.
63. Koopman JS, Jacquez JA, Welch GW, et al. The role of early HIV infection in the spread of HIV through populations. *J Acquir Immune Defic Syndr Hum Retrovirol* 1997;14:249–58.
64. Homer JB, Hirsch GB. System dynamics modeling for public health: background and opportunities. *Am J Public Health* 2006;96:452–8.
65. Sterman JD. Learning from evidence in a complex world. *Am J Public Health* 2006;96:505–14.
66. Epstein JM, Goedecke DM, Yu F, et al. Controlling pandemic flu: the value of international air travel restrictions. (Electronic article). *PLoS ONE* 2007;2:e401.
67. Koopman J. Modeling infection transmission. *Annu Rev Public Health* 2004;25:303–26.
68. Wilson WG. Resolving discrepancies between deterministic population models and individual-based simulations. *Am Nat* 1998;151:116–34.
69. Koopman J. Models of infectious disease agent study. (Abstract). *Am J Epidemiol* 2006;163(suppl):S172.
70. Parker DC, Manson SM, Janssen MA, et al. Multi-agent systems for the simulation of land-use and land-cover change: a review. *Ann Assoc Am Geogr* 2003;93:314–37.
71. Brown DG, Riolo R, Robinson DT, et al. Spatial process and data models: toward integration of agent-based models and GIS. *J Geogr Syst* 2005;7:25–47.
72. Fahse L, Wissel C, Grimm V. Reconciling classical and individual-based approaches in theoretical population ecology: a protocol for extracting population parameters from individual-based models. *Am Nat* 1998;152:838–52.