Scientific publications without ODD model descriptions

Supplemental material for Exercise 2, Chapter 3 of *Agent-Based and Individual-Based Modeling*

In selecting these examples we gave priority to those freely available for download. They have not all been carefully reviewed and (intentionally) are not necessarily “good” examples.

Additional example models in particular fields can be found for searching for reviews of agent-based models—there are many. Just a few examples of reviews are:


People interested in economics and finance are encouraged to look for additional publications at Dr. Leigh Tesfatsion’s Agent-based Computational Economics web site: http://www2.econ.iastate.edu/tesfatsi/aappl.htm


Despite tendencies toward convergence, differences between individuals and groups continue to exist in beliefs, attitudes, and behavior. An agent-based adaptive model reveals the effects of a mechanism of convergent social influence. The actors are placed at fixed sites. The basic premise is that the more similar an actor is to a neighbor, the more likely that that actor will adopt one of the neighbor's traits. Unlike previous models of social influence or cultural change that treat features one at a time, the proposed model takes into account the interaction between different features. The model illustrates how local convergence can generate global polarization. Simulations show that the number of stable homogeneous regions decreases with the number of features, increases with the number of alternative traits per feature, decreases with the range of interaction, and (most surprisingly) decreases when the geographic territory grows beyond a certain size.


A scientific methodology in general should provide two things: first, a means of explanation and, second, a mechanism for improving that explanation. Agent-based modelling (ABM) is a method that facilitates exploring the collective effects of individual action selection. The explanatory force of the model is the extent to which an observed meta-level phenomenon can be accounted for by the behaviour of its micro-level actors. This article demonstrates that this methodology can be applied to the biological sciences;
agent-based models, like any other scientific hypotheses, can be tested, critiqued, generalized or specified. We review the state of the art for ABM as a methodology for biology and then present a case study based on the most widely published agent-based model in the biological sciences: Hemelrijk’s DomWorld, a model of primate social behaviour. Our analysis shows some significant discrepancies between this model and the behaviour of the macaques, the genus used for our analysis. We also demonstrate that the model is not fragile: its other results are still valid and can be extended to compensate for these problems. This robustness is a standard advantage of experiment-based artificial intelligence modelling techniques over analytic modelling.


We model opinion dynamics in populations of agents with continuous opinion and uncertainty. The opinions and uncertainties are modified by random pair interactions. We propose a new model of interactions, called relative agreement model, which is a variant of the previously discussed bounded confidence. In this model, uncertainty as well as opinion can be modified by interactions. We introduce extremist agents by attributing a much lower uncertainty (and thus higher persuasion) to a small proportion of agents at the extremes of the opinion distribution. We study the evolution of the opinion distribution submitted to the relative agreement model. Depending upon the choice of parameters, the extremists can have a very local influence or attract the whole population. We propose a qualitative analysis of the convergence process based on a local field notion. The genericity of the observed results is tested on several variants of the bounded confidence model.


Long implicated in the invasion process, live-bait anglers are highly mobile species vectors with frequent overland transport of fishes. To test hypotheses about the role of anglers in propagule transport, we developed a social-ecological model quantifying the opportunity for species transport beyond the invaded range resulting from bycatch during commercial bait operations, incidental transport, and release to lake ecosystems by anglers. We combined a gravity model with a stochastic, agent-based simulation, representing a 1-yr iteration of live-bait angling and the dynamics of propagule transport at fine spatiotemporal scales (i.e., probability of introducing n propagules per lake per year). A baseline scenario involving round goby (Neogobius melanostomus) indicated that most angling trips were benign; irrespective of lake visitation, anglers failed to purchase and transport propagules (benign trips, median probability P = 0.99912). However, given the large number of probability trials (4.2 million live-bait angling events per year), even the rarest sequence of events (uptake, movement, and deposition of propagules) is anticipated to occur. Risky trips (modal P = 0.00088 trips per year; ≈1 in 1136) were sufficient to introduce a substantial number of propagules (modal values, Poisson model = 3715 propagules among 1288 lakes per year; zero-inflated negative binomial model = 6722 propagules among 1292 lakes per year). Two patterns of lake-specific introduction risk emerged. Large lakes supporting substantial angling activity experienced propagule pressure likely to surpass demographic barriers to establishment (top 2.5% of lakes with modal outcomes of five to 76 propagules per year; 303 high-risk lakes with three or more propagules per year). Small or remote lakes were less likely to receive propagules; however, most risk distributions were leptokurtic with a long right tail, indicating the rare occurrence of high propagule loads to most waterbodies. Infestation simulations indicated that the number of high-risk waterbodies could be as great as 1318 (zero-inflated negative binomial), whereas a 90% reduction in bycatch from baseline would reduce the modal number of high risk lakes to zero. Results indicate that the combination of invasive bycatch and live-bait anglers warrants management concern as a species vector, but that risk is confined to a subset of individuals and recipient sites that may be effectively managed with targeted strategies.

This article presents an agent-based computational model of civil violence. Two variants of the civil violence model are presented. In the first a central authority seeks to suppress decentralized rebellion. In the second a central authority seeks to suppress communal violence between two warring ethnic groups.


New epidemics of infectious diseases can emerge any time, as illustrated by the emergence of chikungunya virus (CHIKV) and Zika virus (ZIKV) in Latin America. During new epidemics, public health officials face difficult decisions regarding spatial targeting of interventions to optimally allocate limited resources. We used a large-scale, data-driven, agent-based simulation model (ABM) to explore CHIKV mitigation strategies, including strategies based on previous DENV outbreaks. Our model represents CHIKV transmission in a realistic population of Colombia with 45 million individuals in 10.6 million households, schools, and workplaces. Our model uses high-resolution probability maps for the occurrence of the Ae. aegypti mosquito vector to estimate mosquito density in Colombia. We found that vector control in all 521 municipalities with mosquito populations led to 402,940 fewer clinical cases of CHIKV compared to a baseline scenario without intervention. We also explored using data about previous dengue virus (DENV) epidemics to inform CHIKV mitigation strategies. Compared to the baseline scenario, 314,437 fewer cases occurred when we simulated vector control only in 301 municipalities that had previously reported DENV, illustrating the value of available data from previous outbreaks. When varying the implementation parameters for vector control, we found that faster implementation and scale-up of vector control led to the greatest proportionate reduction in cases. Using available data for epidemic simulations can strengthen decision making against new epidemic threats.


Markets for domestic housing in countries like England differ from other markets because the stock is fixed in the short term, buyers need to raise mortgages to finance their purchases and prices tend to be set through intermediaries (‘estate agents’ or realtors). We introduce an agent-based model in which some of the main features of the English market emerge from interactions between buyers, realtors and sellers and use this model to investigate shocks to the market.


While men have always received more education than women in the past, this gender imbalance in education has turned around in large parts of the world. In many countries, women now excel men in terms of participation and success in higher education. This implies that, for the first time in history, there are more highly educated women than men reaching the reproductive ages and looking for a partner. We develop an agent-based computational model that explicates the mechanisms that may have linked the reversal of gender inequality in education with observed changes in educational assortative mating. Our model builds on the notion that individuals search for spouses in a marriage market and evaluate potential candidates based on preferences. Based on insights from earlier research, we assume that men and women prefer partners with similar educational attainment and high earnings prospects, that women tend to prefer
men who are somewhat older than themselves, and that men prefer women who are in their mid-twenties. We also incorporate the insight that the educational system structures meeting opportunities on the marriage market. We assess the explanatory power of our model with systematic computational experiments, in which we simulate marriage market dynamics in 12 European countries among individuals born between 1921 and 2012. In these experiments, we make use of realistic agent populations in terms of educational attainment and earnings prospects and validate model outcomes with data from the European Social Survey. We demonstrate that the observed changes in educational assortative mating can be explained without any change in male or female preferences. We argue that our model provides a useful computational laboratory to explore and quantify the implications of scenarios for the future.


People who inject drugs (PWID) are at high risk for blood-borne pathogens transmitted during the sharing of contaminated injection equipment, particularly hepatitis C virus (HCV). HCV prevalence is influenced by a complex interplay of drug-use behaviors, social networks, and geography, as well as the availability of interventions, such as needle exchange programs. To adequately address this complexity in HCV epidemic forecasting, we have developed a computational model, the Agent-based Pathogen Kinetics model (APK). APK simulates the PWID population in metropolitan Chicago, including the social interactions that result in HCV infection. We used multiple empirical data sources on Chicago PWID to build a spatial distribution of an in silico PWID population and modeled networks among the PWID by considering the geography of the city and its suburbs. APK was validated against 2012 empirical data (the latest available) and shown to agree with network and epidemiological surveys to within 1%. For the period 2010–2020, APK forecasts a decline in HCV prevalence of 0.8% per year from 44(±2)% to 36(±5)%, although some sub-populations would continue to have relatively high prevalence, including Non-Hispanic Blacks, 48(±5)%. The rate of decline will be lowest in Non-Hispanic Whites and we find, in a reversal of historical trends, that incidence among non-Hispanic Whites would exceed incidence among Non-Hispanic Blacks (0.66 per 100 per years vs 0.17 per 100 person years). APK also forecasts an increase in PWID mean age from 35(±1) to 40(±2) with a corresponding increase from 59(±2)% to 80(±6)% in the proportion of the population >30 years old. Our studies highlight the importance of analyzing subpopulations in disease predictions, the utility of computer simulation for analyzing demographic and health trends among PWID and serve as a tool for guiding intervention and prevention strategies in Chicago, and other major cities.


Complex systems modeling can provide useful insights when designing and anticipating the impact of public health interventions. We developed an agent-based, or individual-based, computation model (ABM) to aid in evaluating and refining implementation of behavior change interventions designed to increase physical activity and healthy eating and reduce unnecessary weight gain among school-aged children. The potential benefits of applying an ABM approach include estimating outcomes despite data gaps, anticipating impact among different populations or scenarios, and exploring how to expand or modify an intervention. The practical challenges inherent in implementing such an approach include data resources, data availability, and the skills and knowledge of ABM among the public health obesity intervention community. The aim of this article was to provide a step-by-step guide on how to develop an ABM to evaluate multifaceted interventions on childhood obesity prevention in multiple settings. We used data from 2 obesity prevention initiatives and public-use resources. The details and goals of the interventions, overview of the model design process, and generalizability of this approach for future interventions is discussed.
http://dx.doi.org/10.1098/rsbl.2008.0038

The status of many Gyps vulture populations are of acute conservation concern as several show marked and rapid decline. Vultures rely heavily on cues from conspecifics to locate carcasses via local enhancement. A simulation model is developed to explore the roles vulture and carcass densities play in this system, where information transfer plays a key role in locating food. We find a sigmoid relationship describing the probability of vultures finding food as a function of vulture density in the habitat. This relationship suggests a threshold density below which the foraging efficiency of the vulture population will drop rapidly towards zero. Management strategies should closely study this foraging system in order to maintain effective foraging densities.


A major challenge in the development of computational models of collective behavior is the empirical validation. Experimental data from a spatially explicit dynamic commons dilemma experiment is used to empirically ground an agent-based model. Three distinct patterns are identified in the data. Two naive models, random walk and greedy agents, do not produce data that match the patterns. A more comprehensive model is presented that explains how participants make movement and harvest decisions. Using pattern-oriented modeling the parameter space is explored to identify the parameter combinations that meet the three identified patterns. Less than 0.1% of the parameter combinations meet all the patterns. These parameter settings were used to successfully predict the patterns of a new set of experiments.


One of the central aims of ecology is to identify mechanisms that maintain biodiversity. Numerous theoretical models have shown that competing species can coexist if ecological processes such as dispersal, movement, and interaction occur over small spatial scales. In particular, this may be the case for nontransitive communities, that is, those without strict competitive hierarchies. The classic non-transitive system involves a community of three competing species satisfying a relationship similar to the children's game rock-paper-scissors, where rock crushes scissors, scissors cuts paper, and paper covers rock. Such relationships have been demonstrated in several natural systems. Some models predict that local interaction and dispersal are sufficient to ensure coexistence of all three species in such a community, whereas diversity is lost when ecological processes occur over larger scales. Here, we test these predictions empirically using a non-transitive model community containing three populations of *Escherichia coli*. We find that diversity is rapidly lost in our experimental community when dispersal and interaction occur over relatively large spatial scales, whereas all populations coexist when ecological processes are localized.

http://www.socgenmicrobiol.org.uk/MIC/144/3275/1443275H.HTM

The generic, quantitative, spatially explicit, individual-based model BacSim was developed to simulate growth and behaviour of bacteria. The potential of this approach is in relating the properties of microscopic entities – cells – to the properties of macroscopic, complex systems such as biofilms. Here, the growth of a single *Escherichia coli* cell into a colony was studied. The object-oriented program BacSim is an extension of Gecko, an ecosystem dynamics model which uses the Swarm toolkit for multi-agent simulations. The model describes bacterial properties including substrate uptake, metabolism, maintenance, cell division and death at the individual cell level. With the aim of making the model easily applicable to various bacteria under different conditions, the model uses as few as eight readily obtainable parameters which can be randomly varied. For substrate diffusion, a two-dimensional diffusion lattice is used. For growth-rate-
dependent cell size variation, a conceptual model of cell division proposed by Donachie was examined. A mechanistic version of the Donachie model led to unbalanced growth at higher growth rates, whereas including a minimum period between subsequent replication initiations ensured balanced growth only if this period was unphysiologically long. Only a descriptive version of the Donachie model predicted cell sizes correctly. For maintenance, the Herbert model (constant specific rate of biomass consumption) and for substrate uptake, the Michaelis–Menten or the Best equations were implemented. The simulator output faithfully reproduced all input parameters. Growth characteristics when maintenance and uptake rates were proportional to either cell mass or surface area are compared. The authors propose a new generic measure of growth synchrony to quantify the loss of synchrony due to random variation of cell parameters or spatial heterogeneity. Variation of the maximal uptake rate completely desynchronizes the simulated culture but variation of the volume-at-division does not. A new measure for spatial heterogeneity is introduced: the standard deviation of substrate concentrations as experienced by the cells. Spatial heterogeneity desynchronizes population growth by subdividing the population into parts synchronously growing at different rates. At a high enough spatial heterogeneity, the population appears to grow completely asynchronously.


The use of computer simulated markets with individual adaptive agents in finance is a new, but growing field. This paper explores some of the early works in the area concentrating on a set of some of the earliest papers. Six papers are summarized in detail, along with references to many other pieces of this wide ranging research area. It also covers many of the questions that new researchers will face when getting into the field, and hopefully can serve as a kind of minitutorial for those interested in getting started.


This paper presents a new agent-based financial market. It is designed to be both simple enough to gain insights into the nature and structure of what is going on at both the agent and macro levels, but remain rich enough to allow for many interesting evolutionary experiments. The model is driven by heterogeneous agents who put varying weights on past information as they design portfolio strategies. It faithfully generates many of the common stylized features of asset markets. It also yields some insights into the dynamics of agent strategies and how they lead to market instabilities.


Skeletal muscle is highly responsive to use. In particular, muscle atrophy attributable to decreased activity is a common problem among the elderly and injured/immobile. However, each muscle does not respond the same way. We developed an agent-based model that generates a tissue-level skeletal muscle response to disuse/immobilization. The model incorporates tissue-specific muscle fiber architecture parameters and simulates changes in muscle fiber size as a result of disuse-induced atrophy that are consistent with published experiments. We created simulations of 49 forelimb and hindlimb muscles of the rat by incorporating eight fiber-type and size parameters to explore how these parameters, which vary widely across muscles, influence sensitivity to disuse-induced atrophy. Of the 49 muscles modeled, the soleus exhibited the greatest atrophy after 14 days of simulated immobilization (51% decrease in fiber size), whereas the extensor digitorum communis atrophied the least (32%). Analysis of these simulations revealed that both fiber-type distribution and fiber-size distribution influence the sensitivity to disuse atrophy even though no single tissue architecture parameter correlated with atrophy rate. Additionally,
software agents representing fibroblasts were incorporated into the model to investigate cellular interactions during atrophy. Sensitivity analyses revealed that fibroblast agents have the potential to affect disuse-induced atrophy, albeit with a lesser effect than fiber type and size. In particular, muscle atrophy elevated slightly with increased initial fibroblast population and increased production of TNF-α. Overall, the agent-based model provides a novel framework for investigating both tissue adaptations and cellular interactions in skeletal muscle during atrophy.


Many animals gain benefits from living in groups, such as a dilution in predation risk when they are closely aggregated (referred to as the 'selfish herd'). Game theory has been used to predict many properties of groups (such as the expected group size), but little is known about the proximate mechanisms by which animals achieve these predicted properties. We explore a possible proximate mechanism using a spatially explicit, individual-based model, where individuals can choose to rest or forage on the basis of a rule-of-thumb that is dependent upon both their energetic reserves and the presence and actions of neighbours. The resulting behaviour and energetic reserves of individuals, and the resulting group sizes, are shown to be affected both by the ability of the forager to detect conspecifics and areas of the environment suitable for foraging, and by the distribution of energy in the environment. The model also demonstrates that if animals are able to choose (based upon their energetic reserves) between selecting the best foraging sites available and moving towards their neighbours for safety, then this also has significant effects upon individuals and group sizes. The implications of the proposed rule-of-thumb are discussed.


Many factors have been implicated in the decline of Delta Smelt Hypomesus transpacificus in the upper San Francisco Estuary, and the importance of each factor is difficult to determine using field data alone. We describe a spatially explicit, individual-based population model of Delta Smelt configured for the upper estuary. The model followed the reproduction, growth, mortality, and movement of individuals over their entire life cycle on the same spatial grid of cells as the Delta Simulation Model (DSM2) hydrodynamics model. Daily values of water temperature, salinity, and densities of six zooplankton prey types were represented on the spatial grid. Reproduction was evaluated daily, and new individuals were introduced into the model as yolk sac larvae. Growth of feeding individuals was based on bioenergetics and zooplankton densities. Mortality sources included natural mortality, starvation, and entrainment in water diversion facilities. Movement of larvae was determined using a particle tracking model, while movement of juveniles and adults was based on salinity. Simulations were performed for 1995?2005. The baseline simulation was generally consistent with the available data. Predicted daily fractions of larvae entrained and annual fractions of adults entrained were similar in magnitude to data-based estimates but showed less interannual variation. Interannual differences in mean length at age 1 had large effects on maturity and subsequent egg production. Predicted and observed spatial distributions in the fall showed moderately good agreement for extremely low- and high-outflow years. As indicated by the population growth rate, 1998 was the best year and 2001 was the worst year. Water year 1998 (i.e., October 1997??September 1998) was characterized by fast growth in fall 1997, low entrainment, and high stage-specific survival rates, whereas water year 2001 had opposite conditions. Our analysis further shows how multiple factors can operate simultaneously to result in the decline in abundance of Delta Smelt. Received November 9, 2012; accepted April 18, 2013

The concept of resilience is widely promoted as a promising notion to guide new approaches to ecosystem and resource management that try to enhance a system's capacity to cope with change. A variety of mechanisms of resilience specific for different systems have been proposed. In the context of resource management those include but are not limited to the diversity of response options and flexibility of the social system to adaptively respond to changes on an adequate scale. However, implementation of resilience-based management in specific real-world systems has often proven difficult because of a limited understanding of suitable interventions and their impact on the resilience of the coupled social-ecological system. We propose an agent-based modeling approach to explore system characteristics and mechanisms of resilience in a complex resource management system, based on a case study of water use in the Amudarya River, which is a semiarid river basin. Water resources in its delta are used to sustain irrigated agriculture as well as aquatic ecosystems that provide fish and other ecosystem services. The three subsystems of the social-ecological system, i.e., the social system, the irrigation system, and an aquatic ecosystem, are linked by resource flows and the allocation decision making of actors on different levels. Simulation experiments are carried out to compare the resilience of different institutional settings of water management to changes in the variability and uncertainty of water availability. The aim is to investigate the influence of (1) the organizational structure of water management, (2) information on water availability, and (3) the diversity of water uses on the resilience of the system to short and long-term water scarcity. In this paper, the model concept and first simulation results are presented. As a first illustration of the approach the performances of a centralized and a decentralized regime are compared under different scenarios of information on water availability. Under the given conditions of a regularly fluctuating inflow and compliance of agents with orders from a national authority, the centralized system performs better as long as irrigation is the only type of water use. Diversification of resource use, e.g., irrigation and fishing, increases the performance of the decentralized regime and the resilience of both. Systematic analysis of the performance of different system structures will help to identify properties and mechanisms of resilience. This understanding will be valuable for the identification, development, and evaluation of management interventions in specific river basins.


Background. The spontaneous emergence of phenotypic heterogeneity in clonal populations of mammalian cells in vitro is a rule rather than an exception. We consider two simple, mutually non-exclusive models that explain the generation of diverse cell types in a homogeneous population. In the first model, the phenotypic switch is the consequence of extrinsic factors. Initially identical cells may become different because they encounter different local environments that induce adaptive responses. According to the second model, the phenotypic switch is intrinsic to the cells that may occur even in homogeneous environments. Principal Findings. We have investigated the "extrinsic" and the "intrinsic" mechanisms using computer simulations and experimentation. First, we simulated in silico the emergence of two cell types in a clonal cell population using a multiagent model. Both mechanisms produced stable phenotypic heterogeneity, but the distribution of the cell types was different. The "intrinsic" model predicted an even distribution of the rare phenotype cells, while in the "extrinsic" model these cells formed small clusters. The key predictions of the two models were confronted with the results obtained experimentally using a myogenic cell line. Conclusions. The observations emphasize the importance of the "ecological" context and suggest that, consistently with the "extrinsic" model, local stochastic interactions between phenotypically identical cells play a key role in the initiation of phenotypic switch. Nevertheless, the "intrinsic" model also shows some other aspects of reality: The phenotypic switch is not triggered exclusively by the local environmental variations, but also depends to some extent on the phenotypic intrinsic robustness of the cells

Landscape changes can result in habitat fragmentation and reduced landscape connectivity, limiting the ability of animals to move across space and altering infectious disease dynamics in wildlife. In this study, we develop and implement an agent-based model to assess the impacts of animal movement behavior and landscape structure on disease dynamics. We model a susceptible/infective disease state system applicable to the transmission of feline immunodeficiency virus in bobcats in the urbanized landscape of coastal southern California. Our agent-based model incorporates animal movement behavior, pathogen prevalence, transmission probability, and habitat fragmentation to evaluate how these variables influence disease spread in urbanizing landscapes. We performed a sensitivity analysis by simulating the system under 4200 different combinations of model parameters and evaluating disease transmission outcomes. Our model reveals that host movement behavior and response to landscape features play a pivotal role in determining how habitat fragmentation influences disease dynamics. Importantly, interactions among habitat fragmentation and movement had non-linear and counter-intuitive effects on disease transmission. For example, the model predicts that an intermediate level of non-habitat permeability and directionality will result in the highest rates of between-patch disease transmission. Agent-based models serve as computational laboratories that provide a powerful approach for quantitatively and visually exploring the role of animal behavior and anthropogenic landscape change on contacts among agents and the spread of disease. Such questions are challenging to study empirically given that it is difficult or impossible to experimentally manipulate actual landscapes and the animals and pathogens that move through them. Modeling the relationship between habitat fragmentation, animal movement behavior, and disease spread will improve understanding of the spread of potentially destructive pathogens through wildlife populations, as well as domestic animals and humans.


Agent-based modeling is a technique currently used to simulate complex systems in computer science and social science. Here, we propose its application to the problem of molecular self-assembly. A system is allowed to evolve from a separated to an aggregated state following a combination of stochastic, deterministic, and adaptive rules. We consider the problem of packing rigid shapes on a lattice to verify that this algorithm produces more nearly optimal aggregates with less computational effort than comparable Monte Carlo simulations


A significant problem in wildlife management is identifying “good” habitat for species within the short time frames demanded by policy makers. Statistical models of the response of species presence/absence to predictor variables are one solution, widely known as habitat modeling. We use a “virtual ecologist” to test logistic regression as a means of developing habitat models within a spatially explicit, individual-based simulation that allows habitat quality to influence either fecundity or survival with a continuous scale. The basic question is how good are logistic regression models of habitat quality at identifying habitat where birth rates are high and death rates low (i.e., “source” habitat)? We find that, even when all the important variables are perfectly measured, and there is no error in surveying the species of interest, demographic stochasticity and the limiting effect of localized dispersal generally prevent an explanation of much more than half of the variation in territory occupancy as a function of habitat quality. This is true regardless of whether fecundity or survival is influenced by habitat quality. In addition, habitat models only detect a significant effect of habitat on territory occupancy when habitat quality is spatially autocorrelated. We find
that habitat models based on logistic regression really measure the ability of the species to reach and colonize areas, not birth or death rates.


The epidermal growth factor receptor (EGFR) is frequently overexpressed in many cancers, including non-small cell lung cancer (NSCLC). In silico modeling is considered to be an increasingly promising tool to add useful insights into the dynamics of the EGFR signal transduction pathway. However, most of the previous modeling work focused on the molecular or the cellular level only, neglecting the crucial feedback between these scales as well as the interaction with the heterogeneous biochemical microenvironment.