

# Quantitative Bioscience for the 21st Century

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*Using a carefully chosen set of examples, we illustrate the importance and ubiquity of quantitative reasoning in the biological sciences. The examples range across many different levels of biological organization, from diseases through ecosystems, and the problems addressed range from basic to applied. In addition to the overall theme that mathematical and statistical approaches are essential for understanding biological systems, three particular and interacting mathematical themes emerge. First, nonlinearity is pervasive; second, inclusion of stochasticity is essential; and third, issues of scale are common to all applications of quantitative approaches. Future progress in understanding many biological systems will depend on continued applications and developments in these three areas, and on understanding how nonlinearity, stochasticity, and scale interact.*

*Keywords: mathematics, ecosystems, evolution, mathematical biology, nonlinearity*

**B** iologists are entering a new era in which they require quantitative solutions to large-scale and complex problems. Mathematical advances, particularly in analytical and numerical modeling, statistics, and nonlinear systems analysis, are crucial for finding useful solutions and developing predictive tools for biology. Here we use examples to illustrate why and how mathematical and quantitative approaches are essential for making advances in scientists' understanding of biological processes. Although we touch on ideas spanning the scope of biological research, we focus primarily on the environmental sciences, ecology, and evolution.

Throughout these examples, there are at least three common threads. First, mathematics has been well developed to deal with nonlinear models that are deterministic, or with linear models that include stochasticity. Future advances will require the use and analysis of nonlinear stochastic models (box 1), as illustrated by the studies reviewed by Bjørnstad and Grenfell (2001). In a variety of species, understanding dynamics is impossible with deterministic models alone. Furthermore, because biological systems often seriously violate the assumptions underlying simple methods for analyzing mathematical systems, we still need to develop appropriate working definitions of properties such as stability and resilience (Ives et al. 2003) to characterize observed populations, communities, and ecosystems in ways that answer questions biologists want to ask.

Second, it is imperative that scientists develop new methods, both statistical and mathematical, for understanding how to deduce information from biological data sets, a topic treated in more detail by Green and colleagues (2005). For example, to advance fundamental understanding of principles governing population dynamics, new approaches are needed to obtain an acceptable quantitative fit of biological models

to data. Current methods for obtaining fit that include both stochasticity in the underlying dynamics and errors in observation are still computationally and conceptually challenging (de Valpine 2003). How complex must a model be to reproduce a given set of data? What data are required to validate a given model? How can a model best be used to distinguish among competing explanations of biological phenomena?

Third, much more work is needed to characterize variability across scales of time and space. Can activities distributed across large spatial and temporal scales be understood on the basis of knowledge gained from brief, spatially restricted experimental observations? Ecological communities consist of many interacting species, just as neuronal networks consist of a "population" of interacting neurons. What is the appropriate way to simplify these systems, or, on the other hand, what are the appropriate mathematical tools to understand the full complexity of systems consisting of a large number of strongly interacting cells, organisms, or species?

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### Box 1. Nonlinear stochastic models.

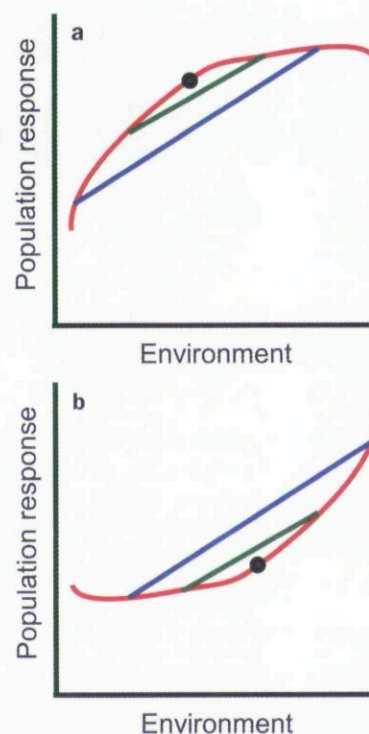
Nonlinearity is a mathematical theme that runs through examples of the application of mathematics to environmental and ecological problems. Jensen's inequality (see Chesson [1985] for an example of its use) is a key concept that allows understanding of the response of some simple nonlinear stochastic models. As illustrated in figure 1, if the response of a key variable to the environment is either concave down (figure 1a) or concave up (figure 1b), the role of variability, and increasing variability, is easy to understand. The simplicity of this result arises because the nonlinearity enters in a simple way. However, it is easy to see that such simple responses will not be found if the response curve is more complex, if there are several dependent variables that interact in a complex way, or if explicit space is included. It is, however, just these kinds of interactions that are pervasive in ecological systems, and therefore further efforts at understanding the interaction between nonlinearity and stochasticity are central to further progress in using mathematics to understand ecological systems.

The large number of ways in which mathematics and statistics have been applied in biological studies makes it impossible to give a sensible, comprehensive survey. Therefore, we have a more limited goal. Instead, we consider particular examples of mathematical applications in the environmental sciences, illustrating the types of problems formulated and solved with the aid of quantitative tools. We have chosen examples in which there is both a history of success and the prospect of new and exciting developments. As we go through these examples, a number of themes emerge, thus giving some generality to our review. In the following section, we will explore some of these themes in more detail. Finally, we will end with some speculations and suggestions for the general research agenda linking mathematics, statistics, and environmental sciences in the 21st century.

### Examples of mathematical and quantitative reasoning in environmental biology

Here we give both a historical perspective and future prospects for a number of examples illustrating the role of mathematical reasoning in environmental biology. We go through these examples roughly in order of increasing level of biological organization, and thereby illustrate the ubiquity of mathematical reasoning at different biological scales.

**Evolution of virulence.** Diseases such as cholera emerge as sudden outbreaks, showing marked variation through space and time both in their *incidence*—the number of individuals infected in a population—and in their *virulence*—the damage a pathogen does to its victim in the course of completing its life cycle. Epidemiologists have long studied how incidence



**Figure 1.** Diagram of the effects of increasing variability on average response when a system is either concave down or concave up, an application of Jensen's inequality. The different lines illustrate the range of responses as the variability increases around a mean value represented by the black dot. As variability increases, the average response can either (a) go down or (b) go up.

of viral, bacterial, and metazoan parasites can fluctuate in response to changes in infectiousness and transmission, which in turn are driven by social, economic, and medical trends. More recently, they have begun to appreciate that virulence is also dynamic, evolving rapidly in response to the same factors that drive pathogen numbers.

The "classical dogma" of epidemiologists was that pathogens always evolve in the direction of lower virulence, eventually becoming harmless symbionts. Evolutionary models have led epidemiologists to abandon this simple assumption, replacing it with a much richer view that incorporates the effects of within-host competition, trade-offs between transmission and virulence, and coevolution between pathogen offenses and host defenses. A strong implication of the trade-off theory, which focuses on the pathogen's trade-off between maximizing its replication and preserving its host's viability, is that public health experts can manage the virulence as well as the incidence of disease by taking actions that lower transmission rates (Dieckmann et al. 2002). Simple mathematical models have been essential in formulating and understanding the conclusions of the trade-off theory (Ewald 1995, Gandon et al. 2001).

The trade-off theory focuses on one particular aspect of host-pathogen coevolution, and it takes a simple phenome-



nological view of the trade-offs constraining pathogen life histories. More sophisticated mathematical analyses have explored the balance between the effects of selection within and between hosts (Frank 1996), the effects of spatial structure (Boots and Sasaki 1999), and the connection between population dynamics and evolution (Lenski and May 1994). Much work remains to be done in formulating and developing these more complex mathematical models, and in finding ways of analyzing them. In particular, spatial disease-evolution models have connections to all of the mathematical challenges (non-linear, stochastic models with spatial or network structure) that are identified elsewhere in this article.

As recent challenges to the trade-off theory have pointed out, existing models may still be too simple and too focused on the phenomenon of parasite trade-offs to come to grips with the reality of virulence evolution. Quantitative biologists must come to grips with a complex, stochastic, poorly observed system; to do so, they will need new analytical tools that incorporate some realistic details and allow for formal matching with data, but still preserve researchers' ability to understand (and therefore generalize) the underlying dynamics of the system. Empiricists in this field have prospected for qualitative virulence factors in the genomes of pathogens, an approach that poorly matches the quantitative framework of most interest to theoreticians (Reid et al. 2000). Theoreticians must work to build models of qualitative genetics, and empiricists must work to establish the mechanistic basis for continuous variation in virulence (Mackinnon and Read 1999a, 1999b). A similar gulf exists between theoreticians and immunologists, with theoreticians wanting to condense immune states down to a single oversimplified axis of immunocompetence, and immunologists insisting that every cell subtype has a unique role that must be reflected in a realistic model (Segel 2001). How do we make our models, in Einstein's words, "as simple as possible, but no simpler"?

**Community ecology of disease.** Ebola, hantavirus, bubonic plague, Lyme disease, West Nile virus, rinderpest, and canine distemper virus are all examples of diseases that affect focal host populations through repeated transmission across species boundaries (Osterhaus 2000, Schmid and Ostfeld 2001, Yates et al. 2002). To understand, predict, and control these diseases, we must understand the ecology of the reservoir host communities that maintain and amplify disease, and the ecology of contacts between these reservoir communities and the focal, or receiving, species. Empirical work is necessary to establish the basic facts of individual-level infection and immunity, as well as the patterns of animal behavior and movement that influence disease spread. Quantitative theoretical models play an essential role in guiding data collection, in estimating transmission rates within and between species (which is almost impossible without a modeling framework), and in understanding the observed patterns of disease. Furthermore, models can be used to assess ways to control disease outbreaks, such as vaccinating, culling, or treating particular reservoir species.

The Serengeti ecosystem, one of the most spectacular biological communities in the world, was devastated when rinderpest was introduced from central Asia in the late 19th century and spread among domesticated and wild ungulate populations. The cascading effects of lowered ungulate population sizes permanently changed the vegetation structure of East Africa, and may have made conditions more suitable for the invasion of tsetse flies (vectors of sleeping sickness), further modifying the biological and human communities of the region. Although these historical effects are still not completely worked out, it is clear that rinderpest, like the related measles virus, is subject to extreme "boom and bust" dynamics and could not maintain itself within the diverse community of wild ungulates in the Serengeti. Instead, rinderpest was maintained by stable populations of domestic cattle surrounding the wild herds. With the development and successful deployment of rinderpest vaccine in domestic cattle, the rinderpest epidemic has been brought under control, and wild ungulate herds have increased to near-historic levels, although some community-level effects of disease may be permanent.

While many diseases have complex dynamics, they also depend on the dynamics of a community of animals, and the latter dynamics are just as complex, if not so well worked out. Ebola spreads among apes as well as humans and is maintained by an as yet unknown animal reservoir; Lyme disease and bubonic plague appear to persist in rodent populations by jumping sporadically among subpopulations (Keeling and Gilligan 2000). In many ways researchers are limited by the difficulty of gathering data on disease in wildlife populations, but another limiting factor is our ability to make sense of the data we do have. We must develop modeling frameworks for multispecies epidemics, possibly by extending existing models that include host subtypes to handle multiple species. We must find better ways of analyzing non-linear multispecies models beyond the existing techniques of (a) linearizing many-species models (Koopman et al. 1989) or (b) doing exhaustive nonlinear analyses of models with no more than three species (Begon et al. 1992). We must adapt methods for estimating transmission rates within species (Bjørnstad et al. 2002) to the much more difficult multispecies case. The biggest challenge in this area, however, is how to use the sparse data we do have. We need techniques to leverage existing data, for example, by using allometric scaling models to constrain the demographic and life-history parameters of different species (De Leo and Dobson 1996), or by using Bayesian methods to include information from other systems, and combine all of these data in a way that accounts for our uncertainties. Only with these tools in hand can we know how effective vaccination, culling, and treatment will be, and where and when to apply them.

**Management of renewable resources.** As the human population has increased, human impacts on resources such as fisheries and forests have continued to grow. Recent developments, including the closure of the groundfish fishery off the West



Coast of the United States and the closure of parts of the Grand Banks off the northeastern United States to certain kinds of fishing, are indicative of the kinds of difficulties that are likely to increase in the future. Although the ideas outlined below apply to many renewable resources, we highlight several problems concerning fisheries for illustrative purposes.

There are basic and well-developed applications of mathematical and quantitative approaches to the management of fisheries. In management, it is important to understand both the biology and the economics of the system (Clark 1990). Further, resource management is a field in which attention to specific assumptions is essential, and the goal is quantitative prediction of how a system might change under different management strategies. For example, the most basic concept in resource management is that of maximum sustainable yield, the largest harvest rate on a population that can be sustained indefinitely. The maximum sustainable yield can be calculated from simple models of population dynamics using elementary calculus. Although this concept is useful in exploring the possibility and consequences of overfishing, its shortcomings highlight the dangers of simple attempts to manage resources. Essentially, these simple models do not incorporate the important roles that economics and stochasticity play in the dynamics of a managed resource, both of which can greatly change outcomes (Clark 1990). Approaches that use only maximum sustainable yield ignore the cost of fishing, the possible alternative uses of the capital used for fishing, and even the possibility of thinking of the fish stock itself as an investment that could potentially be liquidated and its resources invested elsewhere. Clark (1990) explains how these ideas have played an essential role in management of whale fisheries.

Although maximum sustainable yield is an old concept in fisheries management, it is currently being applied in new contexts. For example, maximum sustainable yields are being used to assess mathematically the conservation advantages of different marine reserve designs, in which fishing is prohibited (Hastings and Botsford 1999, Botsford et al. 2001). Here, too, approaches that explicitly take into account more economic issues are likely to prove fruitful.

A more realistic understanding of the spatial management of renewable resources (Sanchirico and Wilen 2001) requires an integration of economic and biological approaches in a spatial context, an inclusion of temporal variability, and an examination of a large number of kinds of fisheries that have not been covered by the current models. Moreover, because targeted species within fisheries typically have dispersal phases in which there are complex interactions between biology and the physical movement of water (which represents a substantial mathematical and computational challenge on its own), there is much room for improved understanding of the recruitment phase of the life cycle of many managed species. Predictions will, of course, depend on good estimates of current biological conditions and population sizes, so further development of statistical approaches is essential.

**Large-scale and global ecology.** Many of today's most pressing problems are regional or global in nature, including, for example, the effects of land cover and land use on endangered species, the consequences of carbon flow in ocean and atmospheric systems for climate change, the effects of climate change on species distributions, and the protection of ecosystems from human threats. Solving these problems is not trivial, in part because the vast majority of empirical work has been done at fairly small scales, both temporal and spatial. Indeed, it is often impractical or impossible to investigate these problems at regional scales (Miller et al. 2004). A further difficulty is that ecosystems are composed of many interacting parts that can exhibit very complex behaviors and may be sensitive to initial conditions and context.

Mathematical and statistical tools are central to enhancing scientists' understanding of large-scale systems and include, for example, cybernetics, control theory, information theory, network theory, thermodynamics, self-organization theory, emergence and hierarchy theory, and power laws (Müller 1992, 1997). A compelling example of the application of mathematical theory to important global-scale ecological problems comes from the work of Allen and colleagues (2002). Historically, one of the most prominent but least understood patterns in nature is the well-known latitudinal gradient in biodiversity from poles to the equator. All major groups of terrestrial, freshwater, and marine taxa display latitudinal gradients in biodiversity, yet the principles underlying the origin and maintenance of these patterns have been elusive. Allen and colleagues (2002) used a theoretical model that quantitatively predicted species diversity from the biochemical kinetics of metabolism. Since temperature varies with latitude, a kinetic model can explain the latitudinal gradients that have highest diversity near the tropics. These results established a thermodynamic basis for the regulation of species diversity and the organization of ecological communities.

There are many challenges that remain for making large-scale ecology a more predictive and quantitative science (Pace and Groffman 1998). To be predictive, theory must be used to extrapolate from the growing amount of data being collected in an increasing number of monitoring programs. The sheer amount of data represents a major challenge, as researchers need efficient computational algorithms to store, analyze, and visualize data, often in different formats and at different resolutions (e.g., pixelated satellite images versus surface-water flow rates through monitoring stations). Beyond this, we need informatics techniques to integrate, synthesize, and mine data to address specific problems using data collected from a broad range of institutions for a broad range of purposes. Many problems arise, such as how to combine qualitative and quantitative information, and how to link multiple types of statistical and mathematical models that operate at different spatial and temporal scales (Benda et al. 2002, Burrows et al. 2002).

**Scaling from individuals to ecosystems.** Models that describe how individual organisms acquire energy and materials, and



how they use them for survival, growth, and reproduction, have the potential to link ecological processes at various levels (Kooijman 2000). Dynamic physiological models that describe the flows of energy and elemental matter through individuals, and models that determine how these flows scale up to higher organizational levels, have several different applications. These models can contribute to life-history theory, impose constraints on the dynamics of populations, and form the foundation for analytically and computationally tractable models of ecosystems (Brown et al. 2004).

Biological oceanographers have long used physiologically based models such as the Droop model, which predicts maximum growth rate on the basis of the internal nutrient concentration within individual plankton cells, to scale biogeochemical dynamics up from the functioning of single foraging plankton to the biogeochemical balances of entire ocean cells; these are then embedded in three-trophic-level (nutrient–phytoplankton–zooplankton, or NPZ) models and incorporated into large-scale computational mixing models to determine the temporal and spatial patterns of global biogeochemical fluxes. Although debate over the appropriate level of model complexity continues (plankton dynamics are complicated by biochemical variation among different plankton guilds and by successional changes in size distribution), the simpler models are routinely embedded in large-scale climate models to predict the effects of plankton growth on atmosphere–ocean carbon balances, and have recently been adapted to study phytoplankton blooms (Sommer 1991, Hurtt and Armstrong 1999, Huppert et al. 2002).

Scaling of biogeochemical fluxes in terrestrial systems has proved much harder. Although ecosystem ecologists often scale “from leaf to globe” in one or two steps (Ehleringer and Field 1993, Fitz et al. 1996), population and community ecologists have insisted that variability within and among populations and species must be incorporated in this scaling process. Such scaling is biologically and mathematically non-trivial. Even when scaling from leaves to individual trees, functional ecologists have found it difficult to develop general models that can predict plant responses to increases in carbon dioxide and temperature (Bernacchi et al. 2000). The problem gets even harder when plants balance their needs for multiple nutrients; interact with other plants, soil microbes, or herbivores; respond to their environment by acclimating (showing phenotypic plasticity); or respond by changing their development (showing ontogenetic shifts). Scientists and managers need the data, and the models to interpret the data, to understand the effects of spatially dispersed environmental disturbances (Moorcroft et al. 2001), successional and climate-driven shifts of species composition within a given habitat, and movement of species range limits when climates change rapidly (Pitelka et al. 1997).

The mathematical, statistical, and computational challenges here are formidable. Scientists must come up with ways of reliably constraining large models with continental-scale databases, and of estimating the future behavior of species assemblages in a changing climate. More fundamen-

tally, we need to find models and methods of solution that are quick enough to be coupled with global-scale simulation models, through some combination of computational advances (algorithmic and parallel-computation techniques) and mathematical advances that aggregate the details of models while retaining quantitative accuracy in physical and biogeochemical properties at a larger scale.

The critical biological question is whether the signature of individual interactions with the abiotic environment is reliably transmitted up multiple levels of organizational scale, or whether the frequency-dependent and idiosyncratic nature of community interactions blurs these regularities at the ecosystem scale. With sufficient attention to the mathematical rules of scaling, and to the regularities observed in the way that broad classes of organisms have solved their ecological problems (Reich et al. 1997), we should be able to develop a new class of tools that increase our power to understand and predict biological dynamics across a range of scales.

## Conclusions

If the examples described above were not connected by common quantitative and mathematical approaches, prospects for the future would be much bleaker. Biological questions have historically opened up new areas in mathematics and statistics, which in turn have proved useful in other areas of biology. For example, in addition to his invention of a new field of statistics (analysis of variance) for interpreting the results of biological experiments, Sir Ronald Fisher opened up new areas of mathematical analysis through his interest in the traveling waves of invasion of novel genes. Thus, the common themes that run through challenges in quantitative biology should foster new quantitative approaches that will have impacts across a range of biological issues. Here we discuss three themes: spatial and temporal variability, statistical integration of theory and data, and the problem of scaling.

The ubiquity of variability in biological systems has always been known, and yet methods for dealing with stochastic systems are only now reaching a form in which they can easily be applied to models of biological systems, and further development is urgently needed. Stochasticity is present at all levels in environmental biology, ranging from genetic mutations through individual behaviors, movement of individuals, demographic rates (survival and reproduction), population sizes, resource availability, community composition, rates of nutrient fluxes, and the multitude of environmental drivers that affect biological processes. Identifying the underlying processes that affect biological systems requires an explicit accounting of the stochastic nature of the system dynamics. This accounting is also needed to forecast changes in biological systems.

Stochasticity can occur either in space or in time, but in either case it can have large, direct impacts on ecological and evolutionary processes. For example, stochasticity in space, or spatial heterogeneity, can help to explain why there is so much biodiversity on the planet. What allows the estimated 10 million species of higher organisms to coexist on Earth?



Simple laboratory experiments demonstrate how hard it is for similar species to coexist (Lotka 1925, MacArthur and Levins 1967), thus suggesting that the variability of natural systems is responsible for the coexistence of similar species. Recent theoretical advances have shown how spatial and temporal stochasticity can lead to coexistence of competing species that in the absence of stochasticity would not coexist (Chesson 1985, Ives and May 1985). This occurs because competition is inherently a nonlinear process: when averaging variable population growth rates that are nonlinear in space or time, the consequence of stochasticity may be to favor, on average, the rare species, thus facilitating the coexistence of many species in an ecosystem.

A second theme running throughout quantitative biology is that theory needs to be challenged directly with data. This requires statistically fitting models to data, and then using the models to address specific theoretical hypotheses. By building multiple models around different hypotheses and statistically competing the models against each other, statistical inferences can be made about the strength and likelihood of different hypotheses. Furthermore, if models are used to make predictions, rigorous statistical approaches provide not only predictions but also estimates of the confidence that can be placed in the predictions. While statistical confidence is well known and well studied in simple statistical models, obtaining statistical confidence for the predictions from the complex, nonlinear models needed for many biological problems is not simple.

This second theme of challenging theory with data goes hand in hand with the first theme of modeling spatial and temporal variability. In a statistical model for biological systems, accounting generally has to be made for *process variability* (the "true" stochasticity of the biological processes, which essentially represents all those factors not included in a model) and *observation variability* (uncertainty introduced by researchers' inability to observe the "true" system perfectly). To address our first theme (integrating theory with data), the challenge is to produce models that elucidate the effects of process variability on the properties of a biological system. To address the second theme (challenging theory with data), the challenge is to couple this understanding of dynamics with an appropriate description of our limited knowledge of real systems, to produce a statistical model with both process and observation variability. Thus, the second theme has many of the same issues as the first, but is complicated by the need to model how well we can or cannot observe biological systems.

The third theme that is common throughout quantitative biology is the problem of scaling. Questions of scale include the appropriate spatial and temporal resolution needed to address a problem. For example, most ecological systems experience temporal variability in the environment, operating as daily, yearly, and decadal cycles. If ecological systems were purely linear, then the consequences of cyclic fluctuations at these different frequencies would be easy to separate. However, ecological systems are not linear, and therefore the consequences of these different temporal scales and their

interactions are complex. This complexity, which is further complicated by stochasticity, may itself play out differently at different scales. For example, predictions over very short or very long time scales may be easier than predictions over the intermediate time scales that may be of the greatest biological interest. Similar complexities arise in scaling up processes spatially, when interactions at local scales (between individual trees, for example) do not extrapolate easily to patterns observed at regional scales (the species composition of forests).

The issue of scale in quantitative biology involves not just the appropriate spatial and temporal resolution but also the level of detail needed to describe and predict biological processes. Thus, issues of stochasticity present further difficulties in choosing an appropriate scale. For example, for an applied problem such as the design of marine reserves, is it most appropriate to lump fish species into generic categories (planktivores, piscivores, top predators), to treat each species separately, or to treat each individual fish separately? The answer to this question depends in part on how the ecological system works. For example, are species of planktivores similar enough that they can be lumped, or are there differences that affect optimal reserve designs? This depends on nonlinearities in the dynamics of individual species, and on how these nonlinearities interact with stochastic forces that affect the system. But it also depends on what data are available. If data are not available for separate species of planktivores, then it might make no sense to build a model with separate species. Thus, the third theme of scale ties directly to the two other themes of quantitative biology: (1) the effects of variability in nonlinear systems and (2) the statistical fitting of theoretical models with data.

Across all of these themes, one goal rises as paramount. No model gives a true depiction of a biological system; a model is by definition an approximation, a caricature of reality (e.g., Lotka-Volterra competition models). This is obviously true of intentionally simple models that are designed to give crude but general understanding of biological processes. It is less obviously but no less true for complex, highly parameterized models tailored for specific biological systems (e.g., CENTURY; Parton et al. 1995). Thus, quantitative biology is inherently limited to inferences made from approximations to real systems. Acknowledging this limitation, the main goal of quantitative biology should be to derive not just predictive models of specific systems but also simple generalities and rules of thumb that transcend the details of the mathematics. Ultimately, mathematical models must benefit biologists by clarifying the problems they address, and the yardstick of mathematical modeling in biology must be the insight it gives into biological systems, rather than the elegance of mathematical solutions.

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## References cited

- Allen AP, Brown JH, Gillooly JF. 2002. Global biodiversity, biochemical kinetics, and the energetic-equivalence rule. *Science* 297: 1545–1548.
- Begon M, Bowers RG, Kadianakis N, Hodgkinson DE. 1992. Disease and community structure: The importance of host self-regulation in a host–host–pathogen model. *American Naturalist* 139: 1131–1150.
- Benda LE, Poff L, Tague C, Palmer MA, Pizzuto J, Cooper S, Stanley E, Moglen G. 2002. How to avoid train wrecks when using science in environmental problem solving. *BioScience* 52: 1127–1136.
- Bernacchi CJ, Coleman JS, Bazzaz FA, McConaughay KDM. 2000. Biomass allocation in old-field annual species grown in elevated CO<sub>2</sub> environments: No evidence for optimal partitioning. *Global Change Biology* 6: 855–863.
- Bjørnstad ON, Grenfell BT. 2001. Noisy clockwork: Time series analysis of population fluctuations in animals. *Science* 293: 638–643.
- Bjørnstad ON, Finkenstadt BF, Grenfell BT. 2002. Dynamics of measles epidemics: Estimating scaling of transmission rates using a time series SIR model. *Ecological Monographs* 72: 169–184.
- Boots M, Sasaki A. 1999. 'Small worlds' and the evolution of virulence: Infection occurs locally and at a distance. *Proceedings: Biological Sciences* 266: 1933–1938.
- Botsford LW, Hastings A, Gaines SD. 2001. Dependence of sustainability on the configuration of marine reserves and larval dispersal distance. *Ecology Letters* 4: 144–150.
- Brown JH, Gillooly JF, Allen AP, Savage VM, West GB. 2004. Toward a metabolic theory of ecology. *Ecology* 85: 1771–1789.
- Burrows SN, Gower ST, Clayton MK, Mackay DS, Ahl DE, Norman JM, Diak G. 2002. Application of geostatistics to characterize leaf area index (LAI) from flux tower to landscape scales using a cyclic sampling design. *Ecosystems* 5: 667–679.
- Chesson PL. 1985. Coexistence of competitors in spatially and temporally varying environments: A look at the combined effects of different sorts of variability. *Theoretical Population Biology* 28: 263–287.
- Clark CW. 1990. *Mathematical Bioeconomics: The Optimal Management of Renewable Resources*. 2nd ed. New York: Wiley.
- De Leo GA, Dobson AP. 1996. Allometry and simple epidemic models for microparasites. *Nature* 379: 720–722.
- de Valpine P. 2003. Better inferences from population-dynamics experiments using Monte Carlo state–space likelihood methods. *Ecology* 84: 3064–3077.
- Dieckmann U, Metz JAJ, Sabelis MW, Sigmund K, eds. 2002. *Adaptive Dynamics of Infectious Diseases: In Pursuit of Virulence Management*. Cambridge (United Kingdom): Cambridge University Press.
- Ehleringer JR, Field CB, eds. 1993. *Scaling Physiological Processes: Leaf to Globe*. New York: Academic Press.
- Ewald PW. 1995. The evolution of virulence: A unifying link between parasitology and ecology. *Journal of Parasitology* 81: 659–669.
- Fitz HC, Debellevue EB, Costanza R, Boumans R, Maxwell T, Wainger L, Sklar FH. 1996. Development of a general ecosystem model for a range of scales and ecosystems. *Ecological Modelling* 88: 263–295.
- Frank SA. 1996. Models of parasite virulence. *Quarterly Review of Biology* 71: 37–78.
- Gandon S, Mackinnon MJ, Nee S, Read AF. 2001. Imperfect vaccines and the evolution of pathogen virulence. *Nature* 414: 751–756.
- Green JL, et al. 2005. Complexity in ecology and conservation: Mathematical, statistical, and computational challenges. *BioScience* 55: 501–510.
- Hastings A, Botsford LW. 1999. Equivalence in yield from marine reserves and traditional fisheries management. *Science* 284: 1537–1538.
- Huppert A, Blasius B, Stone L. 2002. A model of phytoplankton blooms. *American Naturalist* 159: 156–171.
- Hurtt GC, Armstrong RA. 1999. A pelagic ecosystem model calibrated with BATS and OWSI data. *Deep-sea Research: Oceanographic Research Papers* 46: 27–61.
- Ives AR, May RM. 1985. Competition within and between species in a patchy environment: Relations between microscopic and macroscopic models. *Journal of Theoretical Biology* 115: 65–92.
- Ives AR, Dennis B, Cottoingham KL, Carpenter SR. 2003. Estimating community stability and ecological interactions from time-series data. *Ecological Monographs* 73: 301–330.
- Keeling MJ, Gilligan CA. 2000. Bubonic plague: A metapopulation model of a zoonosis. *Proceedings: Biological Sciences* 267: 2219–2230.
- Kooijman SALM. 2000. *Dynamic Energy and Mass Budgets in Biological Systems*. 2nd ed. Cambridge (United Kingdom): Cambridge University Press.
- Koopman JS, Longini IM, Jacquez JA, Simon CP. 1989. Structured and selective mixing formulations of heterogeneous contact to study sexually-transmitted diseases. *American Journal of Epidemiology* 130: 838.
- Lenski RE, May RM. 1994. The evolution of virulence in parasites and pathogens: Reconciliation between two competing hypotheses. *Journal of Theoretical Biology* 169: 253–265.
- Lotka AJ. 1925. *Elements of Physical Biology*. Baltimore: Williams and Wilkins.
- MacArthur RH, Levins R. 1967. The limiting similarity, convergence and divergence of coexisting species. *American Naturalist* 101: 377–385.
- Mackinnon MJ, Read AF. 1999a. Genetic relationships between parasite virulence and transmission in the rodent malaria *Plasmodium chabaudi*. *Evolution* 53: 689–703.
- . 1999b. Selection for high and low virulence in the malaria parasite *Plasmodium chabaudi*. *Proceedings: Biological Sciences* 266: 741–748.
- Miller JR, Turner MG, Southwick EAH, Dent CL, Stanley EH. 2004. Spatial extrapolation: The science of predicting ecological patterns and processes. *BioScience* 54: 310–320.
- Moorcroft PR, Hurtt GC, Pacala SW. 2001. A method for scaling vegetation dynamics: The ecosystem demography model (ED). *Ecological Monographs* 71: 557–585.
- Müller F. 1992. Hierarchical approaches to ecosystem theory. *Ecological Modelling* 63: 215–242.
- . 1997. State-of-the-art in ecosystem theory. *Ecological Modelling* 100: 135–161.
- Osterhaus A. 2000. Circulation of viruses and inter-species contaminations in wild animals. *Bulletin de la Société de Pathologie Exotique* 93: 156.
- Pace ML, Groffman PM. 1998. Successes, limitations, and frontiers in ecosystem science: Reflections on the Seventh Cary Conference. *Ecosystems* 1: 137–142.
- Parton WJ, et al. 1995. Impact of climate change on grassland production and soil carbon worldwide. *Global Change Biology* 1: 13–22.
- Pitelka LF, et al. 1997. Plant migration and climate change. *American Scientist* 85: 464–473.
- Reich PB, Walters MB, Ellsworth DS. 1997. From tropics to tundra: Global convergence in plant functioning. *Proceedings of the National Academy of Sciences* 94: 13730–13734.
- Reid SD, Herbelin CJ, Bumbaugh AC, Selander RK, Whittam TS. 2000. Parallel evolution of virulence in pathogenic *Escherichia coli*. *Nature* 406: 64–67.
- Sanchirico JN, Wilen JE. 2001. A bioeconomic model of marine reserve creation. *Journal of Environmental Economics and Management* 42: 257–276.
- Schmid KA, Ostfeld RS. 2001. Biodiversity and the dilution effect in disease ecology. *Ecology* 82: 609–619.
- Segel LA. 2001. Controlling the immune system: Diffuse feedback via a diffuse informational network. *Novartis Foundation Symposium* 239: 31–44.
- Sommer U. 1991. A comparison of the Droop and monod models of nutrient limited growth applied to natural populations of phytoplankton. *Functional Ecology* 5: 535–544.
- Yates TL, et al. 2002. The ecology and evolutionary history of an emergent disease: Hantavirus pulmonary syndrome. *BioScience* 52: 989–998.

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