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Quantifying Risk in Epidemiological and Ecological Contexts

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POPULÄRVETENSKAPLIG SAMMANFATTNING

Aldrig tidigare har den mänskliga populationen varit så stor som den är idag, och med ökande befolkningstätheter ökar också påfrestningen på naturen runt omkring oss. Människans påverkan på ekosystem runt hela jorden är tydlig och arter försvinner idag i en takt som är jämförbar med utdöendehastigheten under de förhistoriska massutdöendena, varav det senaste exempelvis ledde till utplånandet av dinosaurierna. Många röster har höjts för att den här utvecklingen måste bromsas både för de hotade arternas skull, men även för vår egen. Men för att kunna hindra artutdöenden måste man förstå varför och hur de sker, något som inte alltid är uppenbart. Ekosystem och relationerna mellan arterna i dem tenderar att vara komplexa och intrikata; förändringar och störningar kan fortplanta sig genom dem på oväntade sätt och få oanade konsekvenser. Ett exempel på detta är en företeelse som kallas funktionellt utdöende. Det kan kortfattat beskrivas som att en art, på grund av en minskning i populationsstorlek, förlorar en del av sin roll i förhållande till en annan art. Minskningen i antal av den första arten kan leda till det något icke-intuitiva resultatet att den andra arten försvinner från systemet innan den första arten har minskat tillräckligt för att själv försvinna.

Att bedriva forskning om hur artutdöenden uppstår och vad de får för konsekvenser är inte alltid lätt. Komplexiteten och storleken hos systemen betyder oftast att kontrollerade experiment i laboratoriemiljö är en utmaning av praktiska orsaker, och att utföra experimenten på verkliga ekosystem är oftast uteslutet på grund av etiska skäl. Ett alternativ som är vanligt när man ställs inför sådana problem är att istället utföra experimenten på en datormodell, det vill säga en matematisk representation av det naturliga systemet. De fyra artiklarna i den här avhandlingen bygger alla på användandet av datormodeller på något sätt. I de första två artiklarna används de för att beskriva ekologiska system av djur- och växtarter som analyseras för att ta reda på hur vanligt förekommande funktionella utdöenden är.

Syftet med studien som beskrivs i Artikel I var att utforska i hur stor utsträckning en försämring i en arts livsbetingelser leder till funktionellt utdöende, i förhållande till hur ofta det leder till traditionellt utdöende. En uppsättning modeller av näringsvävar (nätverk av predator-byte interaktioner) skapades där var och en av alla arter utsattes för en störning i form av förhöjd mortalitet (dödlighet). Mortaliteten för en art ökades successivt tills ett utdöende skedde. Detta utdöende kunde bestå i att arten som fått mortalitetsökningen dog ut, eller så dog en annan art i samma system ut, dvs ett funktionellt utdöende skedde. Resultaten visade att proportionen funktionella utdöenden var mycket hög i förhållande till det alternativa utfallet—över 80 % var av funktionell typ i de flesta system.

Studien i Artikel II bygger vidare på dessa resultat och utvecklar den till att inbegripa ekologiska nätverk som innehåller varierande grad av mutualism—positiva interaktioner som finns mellan exempelvis växter och pollinerare, eller djur som hjälper växter att sprida fröer. Resultaten från Artikel II visar att i de system som har en intermediär grad av mutualistiska interaktioner i kombination med predator-byte interaktioner återfinns den högsta proportionen av funktionella utdöenden. Man skulle kunna hävda att den här typen av nätverk är mer realistiska än de i Artikel I vilket gör resultaten än mer tänkbara. Det är vanligt att bevarandeinsatser till stor del kretsar kring enstaka hotade djurarter. Men om funktionella utdöenden är lika vanliga i naturen som studierna på modeller av ekosystem visar, så betyder det att ett synsätt där ekosystemet och interaktionerna mellan dess arter ligger i fokus är avgörande för framgångsrika bevarandeinsatser.

Men datormodeller används inte enbart inom den ekologiska forskningen; I de andra två studierna i avhandlingen (Artikel III och IV) används datormodeller istället för att simulera utbrott av smittsamma djursjukdomar bland populationer av tamboskap. Spridningen av smitta mellan värdjur kan precis som ekologiska system liknas vid ett komplext nätverk av intrikata relationer och precis som med artutdöenden är risken för utbrott av smittsamma sjukdomar bland boskap något som blir vanligare i och med människans fortsatta befolkningsökning. Allt eftersom vi blir fler ökar efterfrågan på jordbruksprodukter och populationen av de djur som är inblandade i tillverkningen av dessa blir tätare och större, med ökad smittoris som följd. Utbrott av smitta har alltid en negativ påverkan på djurvälstånd, samt kan potentiellt ha mycket svåra ekonomiska och sociala effekter. Att kunna förutsäga var risken är som högst för utbrott och vilka åtgärder som är mest effektiva för att förhindra dem är därför användbar kunskap.

I många smittspridningsmodeller för boskapsrelaterade sjukdomar är de rumsliga förhållandena mellan gårdarna av stor betydelse. Ett vanligt sätt att uttrycka risken att en infekterad gård smittar en annan är som en funktion av avståndet mellan de två gårdarna. Ett problem uppstår emellertid om gårdarnas position är okänd, något som är fallet i USA. Där är informationen begränsad till enbart antalet gårdar per county (ungefär motsvarande Svenska län). En lösning för att ändå kunna implementera den här typen av modeller i USA, som har använts i tidigare studier, är att förutsätta att gårdarna är slumpmässigt utplacerade inom sina respektive counties gränser. Ett annat alternativ är en nyligen introducerad metod för att generera realistiska rumsliga fördelningar av gårdar i USA med hjälp av lokala variabler som bland annat förekomst av vägar, marktyper, klimat osv. I Artikel III undersöks hur olika resultaten av smittspridningsmodeller som beskriver risken för utbrott av mul- och klövsjuka blir, beroende på vilken underliggande rumslig fördelning gårdarna har. Resultatet ger stöd åt användandet av den mer realistiska rumsliga fördelningen jämfört med den slumpmässiga då den slumpmässiga leder till en underskattning av utbrottsrisken för många stora counties i de västra delarna av USA.

En komplex smittspridningsmodell med en stor underliggande population av gårdar kan lätt bli mycket beräkningsintensiv. I vanliga fall krävs dessutom stora volymer av simuleringar för att man ska kunna dra tillförlitliga slutsatser från dem. Om simuleringarna tar lång tid att genomföra hotas därför användbarheten och den vetenskapliga kvalitén hos resultaten. Ett antal metoder har därför utvecklats för att optimera den typ av explicit spatiala smittspridningsmodell som bland annat används i Artikel III. Vanligast är att modellen förenklas för att öka simuleringshastigheten, något som förstås gör resultaten mindre exakta. I Artikel IV introduceras en ny metod som uppnår samma eller något högre hastigheter som den hittills mest effektiva metoden utan att använda några som helst förenklingar av modellen. Förbättringen uppnås genom att ett rutnät läggs över hela landskapet med gårdar och sedan görs en grov uppskattning av om smitta kan spridas mellan vart och ett av paren av rutor. Bara om smitta kan ske mellan två rutor går man vidare och gör en exakt utvärdering av vilka gårdar i rutorna som blir smittade. På detta sätt undviks ett stort antal beräkningar som hade givit utfallet att ingen gård blir smittad och körtiderna kortas ner avsevärt.

ABSTRACT

The rates of globalization and growth of the human population puts ever increasing pressure on the agricultural sector to intensify and grow more complex, and with this intensification comes an increased risk of outbreaks of infectious livestock diseases. At the same time, and for the same reasons, the detrimental effect that humans have on other species with which we share the environment has never been more apparent, as the current rates of species loss from ecological communities rival those of ancient mass extinction events. In order to find ways to lessen the effects of and eventually solve such problems we need ways to quantify the risks involved, something that can be difficult when for instance the sheer size or sensitivity of the systems makes practical experimentation unsuitable. For these situations mathematical models have become invaluable tools due to their flexibility and noninvasiveness. This thesis presents four works involving the quantification of risk in livestock epidemic and ecological contexts using mathematical models. Two of them deal with extinctions of species within model ecological communities, and how species interactions play a role in the identity of the lost species following perturbations to specific species (Papers I and II). The other two regard how the spatial layout of the underlying population of livestock premises affect the risk of foot and mouth disease outbreaks among farms in the USA, and how models of such outbreaks can be optimized to improve their usefulness (Papers III and IV).

Ecological communities consist of species and the often intricate pattern of interactions between them. These interspecies connections can propagate effects caused by disturbances in one end of the network, through the community via the links, to other parts of the network. In some cases, a reduction in the abundance of one species can cause the extinction of a second species before the first species disappears, something called functional extinction. Despite this, many conservation efforts revolve around simply keeping populations of single species at a high enough level for their own survival. In a model setting, the study of Paper I explores and attempts to quantify how common such functional extinctions are in relation to the alternative outcome that a perturbed species itself becomes extinct. This is done by first constructing stable model food webs describing predator-prey interactions of up to 50 species, parameterized through allometric relationships between metabolic processes and body size. Then the smallest amount of extra mortality that can be applied to each and every species in the web before any species become extinct is determined. The study shows that in these model communities, more often than not (>80%) another species, rather than the species that is subjected to the additional mortality will be the one to become extinct first.

The approach of Paper I is taken further in Paper II by applying the same methodology to ecological networks that include mixtures of both antagonistic (predator-prey) and mutualistic (e.g. pollination and seed dispersal) interactions. The results further reinforce the findings of Paper I, and show that ecological networks containing a mixture of antagonistic and mutualistic interactions are more sensitive to functional extinctions than purely antagonistic or purely mutualistic ones, an important finding considering the diversity of interaction types in natural systems. Furthermore, the type of species found to have the lowest threshold before becoming functionally extinct were those with a mixture of interaction types, such as pollinating insects. Both Paper I and II consolidate the notion that when doing conservation work it is important to have the entire community in mind by considering the population sizes that are viable from a multi-species perspective, rather than just focusing on the minimum population sizes that are viable for the individual species.

In Papers III and IV the focus changes somewhat, from models of ecological systems to models of how infectious livestock disease spread between farms in spatially explicit contexts.

For this kind of model, information about the spatial distribution of the hosts is of course crucial, but not always readily available. In the USA, the only available information about livestock premises demography is aggregated at the county scale, meaning that the spatial distribution of the premises within each county is unknown. However, a method exists to simulate realistic stochastic spatial configurations of premises using a set of predictor variables, such as topology, climate and roads. An alternative approach that have been used previously is to assume a uniformly random spatial distribution of premises within each county. But to what extent does the choice between these two methods affect the model's evaluation of the risk of disease outbreaks? In Paper III, this is analyzed specifically for foot and mouth disease. Through simulated outbreaks and by looking at the reproductive ratio of the disease, the outbreak dynamics within the two different spatial configurations of premises are compared. The results show that there is a clear difference in the risk of outbreaks between them, with the non-uniform distributions showing a general pattern of higher outbreak risk. However this difference is dependent on the size and geographic location of the county that the outbreak start in with larger counties in the west of the US showing a stronger effect.

When running numerical simulations with large scale models such as the one used in Paper III, a considerable amount of replication is usually necessary in order to account for the high degree of stochasticity inherent to the problem. Even further replication is required when performing sensitivity analyses of model parameters or when exploring different scenarios, for instance when trying to determine the optimal control strategy for a disease. For this reason, the amount and quality of results that can be produced by such studies can quickly become limited by the availability of computational resources. Finding ways to optimize the computations involved with regard to simulation time is therefore of great value as it can be directly related to the robustness of the results. In Paper IV, an efficient optimization method for the kind of kernel-based local disease spread model used in paper III is presented. The method revolves around constructing a grid structure that is overlaid on top of the farm landscape and dividing the infection process into two steps, first evaluating if any farms within one of the grid squares can become infected given an over-estimation of the probability of infection, and then only if so, evaluate actual infection of a subset of the farms within the receiving square. The method is compared to similar published methods and is shown to be more efficient in most cases, while also being easy to implement and understand. Furthermore, while other methods often involve approximations of the transmission process in order to improve computational speed, the method of Paper IV is shown to be exact. This is a major advantage, since with an approximative method the extent to which the results are affected by the simplification is unknown unless the effect of the approximation is explicitly quantified. In most cases, such quantification would require extensive simulations with the unsimplified approach, something which of course may not be feasible.

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List of papers

- I. Säterberg, T., Sellman, S., Ebenman, B. 2013.
High frequency of functional extinctions in ecological networks.
Nature 499, 468.
- II. Sellman, S., Säterberg, T., Ebenman, B. 2016.
Pattern of functional extinctions in ecological networks with a variety of interaction types.
Theor. Ecol. 9, 83–94.
- III. Sellman, S., Lindström, T., Tildesley, M.J., Webb, C.T., Wennergren, U. 2018.
The effect of spatial clustering on the spread of foot-and-mouth disease within the US cattle population.
Manuscript.
- IV. Sellman, S., Tsao, K., Tildesley, M.J., Brommesson, P., Webb, C.T., Wennergren, U., Keeling, M.J., Lindström, T. 2018.
Need for Speed: An Optimized Gridding Approach for Spatially Explicit Disease Simulations.
In Review.

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1

Introduction

We are facing a biodiversity crisis. All over the world, ecological communities are being pushed back in competition with humans for living space and resources (Ripple et al., 2017). This has led to current extinction rates estimated to be between 100 to 1000 times greater than pre-human background rates (Pimm et al., 1995). Such high rate of species loss implies that we have entered or are at least on the verge of entering the sixth major mass extinction event in the history of life on Earth; the last one of similar magnitude occurring 65 million years ago (Ceballos et al., 2015).

Simultaneously, as the human population grows, there is an ever increasing demand for animal proteins, and as a response to this the agricultural sector intensifies, with increasing numbers and densities of livestock as a result. This leads to an increase in the vulnerability of entire livestock production systems to outbreaks of infectious disease, a development that, for instance, is clearly reflected in the tremendous increase in the prophylactic use of antibiotics within the livestock industry over the last 70 years (Aarestrup, 2015).

Species loss from ecological communities, and the spread of livestock infectious disease may seem like two distinct and clearly separated research fields, and of course they are - still, they do share some major similarities. From the technical perspective they both involve the study of large, complex, inherently biological systems, meaning that the same techniques can sometimes be useful in both fields. Likewise, it also means that they share some of the same complications when it comes to research involving the systems. Performing empirical experiments on ecological communities or a region's entire farm

population can be logistically problematic, if not impossible, due to the size and complexity of the systems. Further, and perhaps even more importantly, controlled empirical experiments involving species extinctions and epidemics are ethically questionable. Therefore, empirical research involving such systems typically have to be broken down into smaller, more manageable pieces. However, this simplification of a system may eliminate parts of its inherent complexity and important features may be lost in the process. If the research requires an intact system or if the complexity itself is the actual feature of interest, an alternative approach is necessary, one that is both noninvasive and able to encompass the complex nature of the systems. Computer models possess both of these properties and using models as a substitute for real systems have proven to be very useful within epidemiology and ecology.

Regardless of the difficulties involved, it can be argued that because the problems associated with biodiversity in ecological systems and livestock epidemics are almost entirely due to human activities, we have an ethical responsibility to do our best to solve them (Soulé, 1985; Angermeier, 2000; Soulé, Estes, Miller, et al., 2005; Fraser et al., 2013). Considering that the growth of the human population is not expected to slow down until at least 2100 (United Nations, 2017) the risks involved can be expected to increase as well, indicating that research on these topics may be more important than ever.

This thesis includes four papers that make use of computer models for quantitative assessments of risk. The first two papers regard the risk of species extinctions within ecological communities, (Papers I and II). Paper III considers the national-scale risk of a livestock epidemic in the US; and Paper IV introduces a method to improve the efficiency and usefulness of a particular and commonly used modeling framework for livestock diseases. The remainder of the introduction and the method sections treat the two topics of ecology and epidemiology mostly separately.

1.1 Functional extinctions

The problem of biodiversity loss have often been countered with conservation efforts revolving around the preservation of single endangered species (Sabo, 2008). This works well in some cases, but real world examples illustrate that due to loss of inter-species interactions, single species approaches may not always be enough to preserve an ecosystem (Soulé, Estes, Berger, et al., 2003; Soulé, Estes, Miller, et al., 2005). As a species becomes more and more rare, the interactions it has with the other members of the ecological community will typically weaken. If the decline of the species' abundance continues indefinitely, it will at some point become extinct and disappear from the community altogether, possibly causing secondary extinctions and even triggering an extinction cascade or a state shift (Scheffer et al., 2001; Estes, Terborgh, et al., 2011). Sometimes, however, the decline of one species can trigger the extinction of another species even before the first species has completely disappeared, something known as a *functional extinction* (Sätersberg et al., 2013). The name of the concept refers to the fact that the species has lost at least one of its functions in the system—without its direct or indirect support, another species within the same ecological community cannot be present. However, it is worth noting that the species can still play an important role to the remaining members of the community after the extinction event has taken place. An obvious example is when a predator's only prey becomes too rare for the predator species to survive, but other less intuitive examples exist. The role of some species as seed dispersers (McConkey and Drake, 2006; McConkey and O'Farrill, 2016) or pollinators (Anderson et al., 2011), for instance, can become lost before the species itself is close to extinction, putting the plants they interact with at risk. Other evidence from fisheries show that reductions in the abundance of top predators may be an especially common reason for changes that cascade throughout the system (Frank et al., 2005; Daskalov et al., 2007; Casini et al., 2009). Another particularly well-known example, which has been documented in detail, comes from the kelp forests in the Northern Pacific Ocean. Here, reduced numbers of sea otters released much of the predation pressure on sea urchins, causing their abundances to increase dramatically, leading to completely barren sea floors in some areas (Estes, Tinker, et al., 2010).

Papers I and II deals with the concept of functional extinctions and what constitutes ecologically effective population sizes. With the help of model ecosystems the prevalence of functional extinctions and the species' traits associated with them are explored. Paper I deals exclusively with networks containing predators and their prey, while Paper II also include mutualistic interactions such as pollination and seed dispersal.

1.2 Livestock disease

Infectious livestock disease affects both animals and humans in multiple ways, most notably through reduced welfare and well-being, as well as through large economical costs (Tomley and Shirley, 2009). A considerable variety of livestock diseases exists; the World Organisation for Animal Health (OIE) lists no less than 67 major cattle, sheep, goat, swine and avian diseases as being specific hazards for 2018 (OIE, 2018). Livestock disease can spread through a number of different pathways depending on type of disease. Many infections spread through close contact between animals, when droplets and aerosols expelled by infectious individuals are inhaled by healthy animals, or by coming into contact with contaminated equipment or feed. Others spread through vectors, either obligately such as the bluetongue virus through biting midges (MacLachlan et al., 2009) or in addition to other forms of transmission as for instance African swine fever (Costard et al., 2009). A common transmission mechanism in some infectious livestock diseases is the movement of animals between premises. This pathway is of particular importance in diseases with slow development like bovine tuberculosis where the animals show clinical signs late in the development and infection can go undetected for a long time (Menzies and Neill, 2000; Gilbert et al., 2005). But animal movements can also play an important role in the spread of other diseases, as despite being a relatively rare event, its potential for long distance transmission may lead to the introduction of the disease to virgin areas (Lindström, Grear, et al., 2013).

The major focus of the livestock disease-related papers in this thesis, however, is foot and mouth disease (FMD), an extremely contagious viral disease that affects a long list of cloven-hoofed animals such as cattle, swine, sheep and goats (Grubman and Baxt, 2004). Infectious animals breathe out virus-containing aerosols that can spread far between premises, but the virus can also persist in the environment and contaminate equipment, vehicles and animal housing for several days or even months (Paton, Gubbins, et al., 2017). It is endemic in parts of Asia, Africa and the Middle East, but outbreaks sporadically occurs in other parts of the world (Brito et al., 2017). Due to its high infectiousness, an introduction into a susceptible population can have enormous consequences.

There are three main control strategies to limit and stop an outbreak of FMD: movement bans, culling and vaccination (Paton, Sumption, et al., 2009). Movement bans are generally implemented as soon as infection is detected in a region around the infected premises and prevents the introduction of infected animals and vehicles carrying fomites to as yet unaffected herds. Culling and preemptive culling revolves around quickly killing infected animals and removing any potential susceptible hosts in the vicinity around the detected infection, respectively (Tildesley, Bessell, et al., 2009). Typically only a minority of the animals culled during an outbreak will be due to them

actually being infected; most are killed in the process of containing the outbreak to a small geographic area by depriving it of available hosts. Some form of contact tracing is generally employed in order to find premises that have had any form of contact with infectious or at-risk farms (dangerous contacts), and these premises are typically also targeted with some form of control action. Vaccination against FMD is an option during an outbreak either as part of a vaccinate-to-live strategy or as a way to suppress infection before culling takes place at a later point (Pluimers et al., 2002; Tildesley, Savill, et al., 2006). However, according to the Article 8.8.7 of the OIE Terrestrial Animal Health Code, the time period until a country recovers FMD-free status and can resume international trade is doubled (from three to six months) if a vaccination-to-live strategy is employed, as opposed to if all vaccinated animals are also destroyed (OIE, 2017). This, in combination to vaccination being a costly strategy in itself gives an economic incentive against its use, and it is consequently a less common strategy than the other two mentioned (Barnett et al., 2015).

The FMD outbreak in the United Kingdom in 2001 is an illustrative example of how severe an outbreak can become. The final cost was estimated at around £4-12 billion and 4 million livestock, mainly cattle, sheep and pigs were culled—either to limit the spread of the disease or for welfare reasons due to movement bans (Anderson, 2002; Crispin et al., 2002; Laurence, 2002). Of course, there are more than monetary effects following such an event as people lose their livelihoods and watch their animals being killed under very stressful or even traumatic circumstances (Mort et al., 2005).

In the case of an FMD outbreak, knowing how to act and where to optimally target control measures is of utmost importance in order to reduce the risks of a major epidemic. Computer models are powerful tools for contingency planning, and can be used to test out different control actions, or pinpoint geographical high-risk areas of particular concern. FMD has a remarkable potential to spread via airborne aerosols over very long distances (Gloster et al., 2005); some even argue that in an earlier outbreak of FMD in 1981, infection spread by wind 250 km across the English Channel (Sørensen et al., 2001). The disease is often modeled with a kernel based approach, where the probability of infection between an infectious and susceptible farm is a function of the distance between them. A common approach has been to let the kernel function represent all forms of between-premises spread and use records of historical outbreaks to find the parameter values for the kernel that best fit the data (Keeling, Woolhouse, Shaw, et al., 2001; Boender et al., 2010; Hayama et al., 2013).

At around 90 million animals, the \$80 billion USA cattle industry is one of the largest in the world (NASS, 2016). An FMD outbreak here would have the potential for enormous economic and social impacts (Knight-Jones and Rush-ton, 2013). This means that there is a large incentive to develop ways to avoid such a development and the US government is of course keen on minimizing

any risk of an outbreak (APHIS, 2014). Paper III and IV in this thesis are part of an ongoing effort to develop a sophisticated modeling framework with primary focus on FMD. The framework is heavily data-driven and capable of modeling farm-to-farm spread on the continental scale via kernel-based transmission and transmission via explicit modeling of animal shipment processes. The framework will be used to evaluate optimal control strategies relevant to FMD and to identify high-risk areas in order to promote preparedness in the US in case of an outbreak. One difficulty with modeling the spread of infectious livestock disease in the US, however, is the lack of a database of premises locations. Without detailed information of where farms are located, assumptions will have to be made about the spatial distribution of farms. Information do exist about the number of premises and animals at the county level however, so one approach has been to assume a uniformly random spatial distribution of farms within counties (Buhnerkempe et al., 2014). Recently, however, development of the Farm Location and Agricultural Production Simulator (FLAPS) has provided a method to construct realistic spatial distributions of farms (Burdett et al., 2015). The FLAPS uses a set of predictor variables determined from aerial photographs in combination with county-level data to predict a probability surface for farm positions from which the explicit locations of farms for the entire US can be generated. The difference between the dynamics of an FMD outbreak in a homogeneous spatial distribution of farms at the county level and a heterogeneous distribution predicted by FLAPS is not obvious, however. A realistic farm distribution would have a greater degree of spatial clustering compared to a randomized one, meaning that there are concentrated areas where the disease would spread quickly. On the other hand, it is easily conceivable that the outbreak could get stuck in an isolated cluster of farms from where it would not be able to move further. This effect is explored in detail in Paper III.

Using models to improve preparedness for livestock disease outbreaks requires exploring a large amount of potential scenarios, and the stochastic nature of numerical simulations means that a large amount of replication is usually necessary. The process of numerical simulation of large-scale outbreaks can be computationally demanding and very time consuming. This means that without suitable optimizations, the parameter space and amount of scenarios that can be evaluated is limited. Such restrictions lead to less comprehensive investigations of control strategies as well as gaps in the knowledge of the spatial variation in epidemic risk and expected outbreak dynamics. Paper IV introduces a method to improve the computational efficiency of kernel based spatially explicit models commonly used to simulate FMD outbreaks. The method is shown to be as fast or faster than current state of the art methods, and achieves the improvements without introducing any approximations into the epidemic model.

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2

Overview of papers

2.1 Paper I

With Paper I we wanted to add support to the argument that taking a community-oriented approach to the preservation of species is of great importance, and point towards the risks of not doing so. To make this apparent we strove to illustrate through experiments on model food-webs how common it is that a disturbance to one species leads to the extinction of another. An additional aim was to explore if the probability of functional extinctions were related somehow to particular species traits.

In sequentially assembled synthetic food webs with 50 species, parameterized with the use of allometric relationships and using Lotka-Volterra dynamics, extinctions were induced by applying additional mortality to each species in the web. In these webs we found that the probability that a species other than the focal species that received the extra mortality was the first to become extinct was on average 0.72 (Fig. 2.1, a). For another set of food webs modeled after real empirical ecosystems and parameterized in a similar manner, the same probability was on average 0.49 (Fig. 2.1, b). This shows clearly that the risks of functional extinctions in these systems are considerable, and a species' role as direct or indirect support for another member of the ecological community can be lost before the species itself is threatened. The functional extinctions occur in all trophic classes, and indirect extinctions of trophically distant species when mortality was applied to top species was not uncommon, pointing to the presence of substantial top down effects and

Figure 2.1: The proportion of extinction events that are of another species (white and gray) than the focal species (black) in the study of Paper I. The mortality rate of the focal species has been increased until an extinction event happens. The different bars represent the trophic group that the focal species belongs to. Results for synthetic food webs (a) and natural food webs (b). Adapted from Säterberg et al. (2013).

complex interaction pathways. Also, an inverse relationship between body mass and the probability of another species becoming extinct first was found, indicating that species with large body mass are of special importance for functional extinctions.

2.2 Paper II

The aim of this study was to broaden the findings of Paper I to ecological communities that contained varying proportions of mutualistic interactions in addition to those of a pure predator-prey system. We also wanted to explore the concept of functional extinctions within another type of network topology as well as see how intraspecific competition affected the prevalence of functional extinctions. Using the same methodology as in Paper I, we analyzed the proportion of extinction events where another species than the focal species became extinct. Two sets of simulated ecological networks with 50 species were generated, one set using the cascade model (see section 4.1.1). The other set consisted of bipartite networks, a type of network topology with two separate groups of species where the only interspecies interactions occur across the two groups. The proportion of mutualistic links in the networks were 0, 0.3, or 0.7, and the intraspecific competition of the entire webs was

Figure 2.2: Frequency of functional extinctions in the cascade webs of Paper II as a function of the proportion mutualistic links and the strength of the intraspecific competition. Adapted from Sellman et al. (2016).

varied by a factor of 0.5, 1.0 or 2.0. There were clear effects of both degree of mutualism and self-regulation. The webs with intermediate proportion of mutualistic interactions showed higher proportion of functional extinctions, as did the webs with the lowest strength of intraspecific competition (Fig. 2.2). The findings are important as they show that the results from Paper I are valid for ecological networks with a larger variety of interaction types and strengths.

2.3 Paper III

Paper III had the objective of exploring how the risk of epidemic outbreaks of foot and mouth disease (FMD) in the US differs depending on the spatial clustering of the underlying population of premises. Specifically, how does using FLAPS-generated populations (section 4.2.4) affect the risks compared to if the population is uniformly distributed within the counties of the US? The average basic reproduction ratio (section 4.2.2) of each US county was used as an analytical measure of the risk involved with getting a FMD outbreak in that county. This analytical approach was complemented with stochastic

simulations of FMD outbreaks started in every county. The results from both approaches show that the risk of outbreaks becomes higher in many counties when random spatial distribution of premises is exchanged for FLAPS generated landscapes. This effect was most prominent in large counties in the western part of the USA. The results points toward the usefulness of the FLAPS and the importance of realistic spatial representation of premises when using computer models to make FMD risk assessments.

2.4 Paper IV

Stochastic, spatially explicit, livestock disease models can, if the population of premises is large, become very slow. Given that it is not unusual to run hundreds of thousands, or even millions of simulations (see Paper III), this easily turns into a practical problem. Furthermore, and perhaps more importantly, it also becomes a scientific problem if the amount of replicates that is feasible becomes a limiting factor for the kind of questions that the model can answer. Many methods to improve the performance of such simulations are through approximations which introduces an uncertainty into the conclusions that can be drawn from them. The aim of Paper IV was to introduce a method to speed up such simulation models without making any sacrifices on behalf of the model exactness. In the paper we present two exact methods to speed up this specific kind of model and compare them to the fastest method in the literature at the time. One of our new methods is shown to be consistently as fast as or faster than the alternative method. The fact that it is exact and not an approximation of the epidemic process is important because it removes the need for sensitivity analyses and uncertainties in the results. The methods introduced are based on an approach where the entire population of premises is overlaid with a grid consisting of square cells. The efficiency (but not the exactness) of the algorithm is sensitive to the choice of cell size, and we provided a simple method to find a cell size that will give a satisfactory increase in computational speed and make the use of it more straightforward.

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3

Concluding remark

The possibility to meaningfully compare the consequence of alternative approaches is essential for prioritizing in the decision making concerning the most efficient ways to conserve species or control outbreaks of infectious disease. Within both of these areas, there is little room for wrong decisions and the stakes are high. In the work for conservation of biological species, resources are scarce and lost species are not easily reintroduced. For outbreaks of infectious disease, the economic and social consequences can be of considerable magnitude. To enable the evaluation that is the basis of such decision making, the outcomes of the involved approaches must in some way be quantified. For complex systems this is no easy task without the help of computer models as they allow for such evaluations in contexts where practical experiments are unavailable.

The studies included in this thesis all involve ways to use computer models to quantify the risk of specific adverse events in ecological and agricultural systems. Both Paper I and II highlights the importance of taking a multi-species approach when assessing the risk of extinctions in ecological communities. The studies show that the probability of the functional extinction of species is very high both in pure predator-prey systems and systems in which part of the interactions are mutualistic. The implication of this is that the reduction in the abundances of some certain species caused by humans today may result in the unexpected loss of other species. It also means that conservation efforts need to focus on protecting entire ecological systems and the interactions between species rather than specific species themselves. The study of

Paper III illustrates the importance of knowledge of the underlying spatial distribution of premises when making decisions about the control of foot and mouth disease in the US. Using populations that are randomly distributed within the counties will under-predict the risk of outbreaks in some parts of the country which could have dire consequences in the case of an actual outbreak. Paper IV shows that it is possible to optimize the kind of model used for the simulations in Paper III without introducing any additional approximations. This is of major importance for two reasons. Firstly, being able to run plenty of simulations increase the robustness of the results which means that control strategies can be developed with a greater degree of confidence. Second, adding no additional approximations to the model means that the only uncertainty in the results stem from the parameterization of the model and the stochasticity of the modeled transmission process itself.

Although the topics of theoretical ecology and epidemiology are clearly separated, there is also some overlap. For instance, the process of transmission between premises in a landscape can be likened with the spatial dispersal of ecological species. Indeed, the approach used in Paper III and IV to model the spread of infection between farms using a distance kernel can be used to model the invasion of species into new habitats without much modification (Lindström, Håkansson, et al., 2011).

Further, ecological and epidemiological processes are part of the same complex interplay between species that is we refer to as nature. Sometimes modeling of one particular disease requires the inclusion of a wildlife host as a reservoir, for instance badgers in bovine tuberculosis (Fitzgerald and Kaneene, 2013; Smith et al., 2016); or a wildlife vector like biting midges in the spread of bluetongue virus (Brand and Keeling, 2017). In these instances it is conceivable that the epidemiological model could be combined with an explicit ecological model that describes the dynamics of the wildlife species. Often, though, this will not be the case as there is usually too little detailed data available on the wildlife species and the ecological context that it exists in.

Lack of detailed data is a reoccurring problem in ecological research as the collection of it is both difficult and resource demanding. On the other hand, reasonably detailed data is often available for livestock populations and disease outbreaks. The similarities between the two topics might potentially mean that method development and validation that occurs in the sometimes more data-rich context of epidemiological research can spill over to ecology and conservation biology and find use there.

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4

Theory and Methods

4.1 Functional extinctions in model ecosystems (Papers I and II)

Ecological networks are complex structures consisting of species and the interactions between them (Montoya et al., 2006). Historically, the type of interactions that have been given the most attention are the trophic links that describe how energy is passed between species, in other words predator-prey interactions. The set of trophic links in an ecological system is usually referred to as a food-web. However, in natural ecological networks, other kinds of interactions exist as well. Competition between species is one such non-trophic interaction, mutualism as in for instance pollination or seed dispersal another. From a theoretical perspective, perhaps the most fundamental property of any ecological network is its topological structure—who interacts with whom. When the structural layout of the network itself is what is being studied, topological depictions may be enough, e.g. Solé and Montoya (2001) and Dunne et al. (2002). When inquiries go further into the dynamical nature of species interactions however, information about the strengths of the interactions themselves has to be added to the network.

4.1.1 Generating network topology

For realism, it is generally preferred to model the networks after naturally occurring systems, but detailed data is scarce and collecting it is often a time

consuming process. For this reason, modelers often have to resort to artificial networks with a synthetic topology. Although the study in Paper I makes use of some real-world food-webs in order to make the results more robust, both Paper I and II includes artificially generated ecological networks. There are a number of different ways to create more or less realistic topological food-web structures ranging from randomly distributed links on one end of the spectrum to simulating the repeated invasion by new species into a growing community on the other end. In between lies a class of hierarchical models that have been created in order to capture realistic structures, but without simulating the actual emergence of a natural food web. This class includes the cascade model (Cohen et al., 1990) in which the S number of species are ordered $1, \dots, S$. Every species then preys upon each of the species below it in the ordering with some probability that is constant and equal for all species in the community. Perhaps due to its simplicity, the cascade model has been popular and in Paper II it is used to generate model food-webs topologies. Despite its popularity, however, the cascade model has its shortcomings. In particular, the strict criterion that species only prey on species below itself means that neither cannibalism, nor the occurrence of species pairs preying on each other. The niche model (Williams and Martinez, 2000), is an extension of the cascade model in which each species i is assigned a niche value n_i and will prey upon all the species whose niche value falls within a range r_i , centered at a random location within the interval $[r_i/2, n_i]$. This solves the problems of the cascade model making it a more realistic choice, although slightly more complex.

4.1.2 Model ecosystem population dynamics

The population dynamics of an ecological model community is the mathematical machinery that describes how the abundances of the species change over time as they interact with each other. In both Paper I and II, the dynamics were based on the commonly seen generalized Lotka-Volterra equations. They are a set of ordinary differential equations that describe the network dynamics within a model food web that describe the rate of change in abundance N_i per unit time of each species i out of S total species. This rate of change is governed by the intrinsic growth rate r_i and a set of pairwise interaction strengths a_{ij} describing species j 's effect on species i

$$\frac{dN_i}{dt} = N_i \left(r_i - \alpha_{ii} N_i + \sum_{j \neq i}^S \alpha_{ij} N_j \right). \quad (4.1)$$

Or in vector form

$$\frac{d\mathbf{N}}{dt} = \mathbf{X}(\mathbf{r} - \mathbf{A}\mathbf{N}), \quad (4.2)$$

where $\mathbf{N}$ is the vector of species abundances, $\mathbf{X}$ is the identity matrix of size S , $\mathbf{r}$ is the vector of intrinsic growth rates and $\mathbf{A}$ is the matrix of all interaction

strengths. Each element a_{ij} of $\mathbf{A}$ is a measure of the density-dependent effect that species j has on i and is negative if j is a predator of i and positive if j is a prey of i . The diagonal of $\mathbf{A}$ describes the effect that the abundance of a species has on its own growth rate, this intra-specific competition reduces the growth of a species proportionally to its own abundance and stops it from growing indefinitely. The intrinsic growth rate is positive for species that do not strictly need to interact with other species in order to fulfill their energy needs. This commonly means primary producers, but other species groups can be modeled with a positive r_i as well, if there is insufficient data on interactions for instance. For all other species, r_i is negative and reflects the background mortality in absence of interaction with other species or individuals of the same species.

This standard formulation of the generalized Lotka-Volterra equations can easily be extended with additional parameters. Both in Paper I and II, the interaction coefficients a_{ij} for a predator's negative effect on a prey species is weighted by that predator's preference for prey species i . Similarly, the positive effect of the prey species on the predator, a_{ji} , is a function of a_{ij} and a conversion parameter that regulates the efficiency with which the predator converts prey into new predators. Another addition used in the two papers is the inter-specific competition between basal species expressed by letting both a_{ij} and a_{ji} be negative, reflecting the natural competition for nutrients, space and light among primary producers.

The way that interaction strength scales with prey abundance is known as the functional response of the predator. In the generalized Lotka-Volterra equations the functional response scales linearly with the abundance of the prey species as $a_{ij}N_i$. This means that in theory, there is no upper limit to how many prey individuals a single predator can kill and handle as the prey abundance increases; this is known as functional response of type I (Fig. 4.1). The Rosenzweig-MacArthur model is an extension of the generalized Lotka-Volterra system that implements nonlinear functional responses (Rosenzweig and MacArthur, 1963),

$$\begin{aligned} \frac{dN_i}{dt} = & N_i b_i - N_i \sum_j^S a_{ij} N_j \\ & - N_i^q \sum_j^S \left[\frac{h_{ij} \alpha_{ij} N_j}{1 + T \sum_{k \in R_j} (h_{kj} \alpha_{kj} N_k^q)} \right] \\ & + N_i \sum_j^S \left[\frac{h_{ji} \alpha_{ji} N_j^q e}{1 + T \sum_{k \in R_i} (h_{ki} \alpha_{ki} N_k^q)} \right] \end{aligned} \quad (4.3)$$

using the same notation as eq. 4.1 except that here α_{ij} is the intrinsic attack rate of consumer species j on its resource i and the elements a_{ij} are strengths of competition (inhibition) of species j on i . The parameter h_{ij} is the pref-

Figure 4.1: Schematic visualization of functional response types. Functional response of type II includes predator handling times or satiation by describing the interaction strength as a function that levels off at high prey abundances. The sigmoid Type III a mechanism for prey to escape predation at low prey densities.

erence that predator j has for resource i and sums to one for every j ; e is the conversion efficiency, R_i and R_j are the sets of resource species for i and j respectively. The capture and handling time T and capture coefficient q , together with the attack rate, determines the shape of the functional response curve Holling (1959). The linear form of type I has an advantage in its simplicity, allowing an analytical approach to find points of local stability (see below), a fact that is leveraged in both Paper I and II. Functional response of type II and III (Fig. 4.1) can arguably be more realistic in many situations, but their nonlinearity generally requires numerical methods when analyzing. The first term in eq. 4.3 represents the intrinsic rate of change in abundance for species i in absence of interactions, the second term is the effect of intra- and inter-species competition on the rate of change. The third and fourth terms represents the negative effects that consumers have on species i and the positive effects that i 's resources have on i . In order to analyze food webs with nonlinear functional response, equation 4.3 was implemented in Paper I in addition to the generalized Lotka-Volterra equations.

4.1.3 Parameterization and stability

Adding any kind of dynamics to a ecological model network of course necessitates some form of quantification of the strengths and effects that the interactions have on the species involved. Measures of per-capita interac-

tion strengths and their distributions from natural ecological communities have been performed in laboratory experiments (Sala and Graham, 2002) and in the field on smaller scales (Paine, 1992). Instead, modelers of ecological systems often use another approach by indirectly inferring parameter values based on the fact that real-world ecological communities are stable in the sense that they are stable and the species in them does not generally become extinct without perturbations from the outside. If a set of parameter values can be found and the ecological system that is being modeled can exist using those parameters, then surely they can be considered ecologically relevant in some sense. One way to find such parameters is to simply assign values at random, drawn from some likely interval until a stable community is reached (May, 1972; Pimm, 1980; Yodzis, 1988). The problem with this approach is that as the number of species increase, the probability of finding a stable solution decreases, meaning that this approach is not useful for larger networks. A more sophisticated approach is to utilize the fact that many of the metabolic processes that underlie the ecological interactions, such as feeding rates and intrinsic mortality or birth rates have been shown to be related to the body mass and thermal and metabolic characteristics of the species (Yodzis and Innes, 1992; Rall et al., 2012). The ecosystem can thereby be parameterized based on proxy variables such as mass and body temperature, for which data is more readily abundant and easier to collect (Brose et al., 2006; Berlow et al., 2009).

The stability of an ecosystem can be measured in different ways, but the focus here lies on the concept of local stability around the equilibrium point, which was used as a criterion for stability in both Paper I and II. This is the solution to eq 4.2 where every species' rate of change is zero and is given by

$$\hat{\mathbf{N}}_i = -\mathbf{A}^{-1}\mathbf{r}, \quad (4.4)$$

where $\mathbf{A}^{-1}$ is the inverse of the interaction matrix $\mathbf{A}$. If each species' abundance at equilibrium, $\hat{\mathbf{N}}_i$ is positive, the point is said to be feasible; if not, the set of species cannot coexist at equilibrium with the given parameters, even though mathematically an equilibrium point exists.

4.1.4 Synthetic and empirical systems used

Allometric scaling was used in Paper I to create dynamical food webs where parameter values for the species were inferred from body masses drawn from random intervals. For these webs a sequential assembly method inspired in part by the niche model and in part by Lewis and Law (2007) was used. A starting community of four basal species was used and additional new species was added one by one to that community. First, each species was randomly chosen to belong to one of three trophic groups with equal probability, basal species (primary producer), herbivore, or predator. The new species was given a random body mass from an interval specific to its trophic group, and if it

was a consumer, it was also given an optimal predator-to-prey body mass ratio indicating what prey species body mass (including basal species for herbivores) for which it had the highest preference. Species interaction strengths were then added to the food web based on Lotka-Volterra dynamics and allometric relationships, and the entire system was checked for local stability and feasibility. If the system could exist with the new addition it was kept and a new species was added until a total of 50 species was reached; if not, the new species was discarded and a new attempt was made. This assembly method was not meant to reflecting the natural process of community formation, but it produced communities with high topological similarity to real food webs. Importantly, it provides a method to generate reasonably large food webs (50 species), parameterized such that all species can coexist at equilibrium.

To analyze food web models with nonlinear functional response somewhat simpler, rectangular networks with 9 species and semi-randomly distributed links were generated. They were parameterized without allometric scaling. Instead, mortality rates r for consumers were randomly drawn from a uniform interval. All other parameters of eq. 4.3, including the growth rates for the basal species were set to fixed values.

Paper I also includes eight empirical food webs with between nine to 67 species with detailed information on topological structure and body masses. They were parameterized in the same manner as the sequentially assembled webs.

Paper II includes networks that have mutualistic links in addition to predator-prey interactions in two different classes of network topologies. One class was created using the cascade model and the other class was randomly linked bipartite networks consisting of two separate sets of species with links between the sets (Fig. ?? b). The networks were parameterized by assigning a random number from the interval $[0, 1]$ to the interaction strengths and equilibrium densities and then solve eq. (4.2) for $\mathbf{r}$ (Mougi and Kondoh, 2012; Mougi and Kondoh, 2014).

4.1.5 Determining functional extinctions

A gradual increase in mortality targeting a single species j in an ecological network that is at a locally stable equilibrium point will inevitably push that stable point into a region where one or more species have abundances that are zero or less, causing an extinctions. However, due to the inter-species interactions present in the network, the species that the mortality is applied to is not necessarily the species that will become extinct first. If j and the extinct species, i , are not the same we designate j as being functionally extinct. In a linear system such as described by eqs. 4.1 and 4.2, the additional mortality needed to cause the functional extinction and the identity of the functionally extinct species can be solved analytically. Denoting the extra mortality added to species j as ϵ_j and letting $\mathbf{e}_j$ be a vector with one at element j and zeros

elsewhere,

$$\hat{N}' = -\mathbf{A}^{-1}(\mathbf{r} - \mathbf{e}j\epsilon_j) \quad (4.5)$$

gives the new equilibrium abundances after added mortality. The new equilibrium density for each species i after adding mortality to species j is given by

$$\hat{N}'_i = \hat{N}_i + \epsilon_j \gamma_{ij}, \quad (4.6)$$

where γ_{ij} is an element of $\mathbf{A}^{-1}$. By setting $\hat{N}'_i$ to zero we can solve for the amount of extra mortality ϵ_j that must be added to j in order to cause the extinction of species i . By finding the species i with the lowest corresponding ϵ_j the species that becomes extinct first when the mortality of j increases is determined. If the extinct species is not j itself, j has become functionally extinct. This analytical approach is used in Papers I and II. For the systems with nonlinear functional response in Paper I, the mortality rate is gradually increased in small steps and a numerical solver is used to determine at which point a species becomes extinct in the system.

4.2 Modeling the spread of disease among livestock (Papers III and IV)

4.2.1 The epidemic model framework

The spread of infection through a population of susceptible individuals is a complex process. Rather than modeling each individual's specific reaction to the infection, the population can be divided into compartments or classes according to their current status and have the individuals transition from between the compartments during the course of the infection. The original formulation of this kind of model contains the compartments Susceptible-Infectious-Recovered (Kermack and McKendrick, 1927). It is suitable for infections where long-lasting immunity is conferred upon recovery or where the individual is otherwise removed from the population (e.g. death). For other kinds of infections, the SIR model framework can be easily be modified for instance into SIS for no immunity upon recovery, or SIRS for temporary immunity. Other compartments can also be added such as an exposed class (E) for infections with a latency period before the onset of infectiousness.

The epidemic model used in Papers III and IV is a stochastic, spatially explicit, discrete-time SEIR model; a type of model that is well suited for the modeling of FMD and one that has been a popular choice ever since the 2001 outbreak in the UK (Keeling, Woolhouse, Shaw, et al., 2001; Keeling, Woolhouse, May, et al., 2003; Keeling, 2005; Tildesley and Keeling, 2008; Boender et al., 2010; Rorres et al., 2011; Hayama et al., 2013; Brand, Tildesley, et al., 2015). In this type of model, a premises is commonly regarded as a single infective unit in the perspective of the SEIR-framework. This assumption means that the premises' entire animal population transitions as

one between compartments. This is a reasonable approximation for diseases such as FMD, which spread fast within a dense population. Implicit in this is another assumption, namely that within the premises the animal populations are well mixed, something that in some cases may be a deviation from reality, especially for very large premises. The transition of a premises j from susceptible to exposed at any given time is dependent on the number of infectious premises i in the population, their spatial distribution in relation to j and their transmissibility, T_j as well as the susceptibility of j , S_j . The parameters T and S are functions of the number of animals (and in the case of Paper IV, type of animal, species are not homogenous in this regard, (Donaldson et al., 2001)) on the premises. The spatial aspect of the transmission process is modeled by a kernel function that scales the probability of infection spreading from one premises to another by the distance between them. Generally, this distance dependence is formulated such that each infectious premises exert an infection pressure on every susceptible premises and the pressure decreases monotonically with distance between premises. More specifically, the shape of the kernel determines this distance dependence and will have a large impact on the behavior of the epidemic (Fig. 4.2.1). A kernel with a fat tail will allow distant transmissions with relatively high probability while a kernel with narrow tail will concentrate new infections closer to already infectious farms. All kernel functions used in papers III and IV were taken directly from the primary literature, with the exception of the kernel called *USDOS* in Paper III, which is at the time of writing still unpublished. The remaining five kernel functions were used together with the parameters that they were presented with, no reparameterization was made except for scaling up of transmissibility

in some cases to achieve larger outbreaks. The sources for the kernel functions are, Brand, Tildesley, et al. (2015), Hayama et al. (2013), Buhnerkempe et al. (2014).

After infection has occurred, the premises enters the exposed class for a fixed latency period that varied between two and five days depending on the kernel model, after which the infected premises entered the infectious compartment. Infectiousness was also set to a fixed number of days varying between five and 16 days, also according to kernel in use.

4.2.2 Transmission rates and infection probabilities

Within the model framework, the process of infection moving from an infectious premises i to a susceptible premises j over the course of a period of time δt is described with the transmission rate

$$\lambda_{ij} = T_i S_j H(d_{ij}) \delta t \quad (4.7)$$

where T_i and S_j is the transmissibility and susceptibility of i and j respectively and $H(d_{ij})$ is the distance kernel function. The time resolution δt can be absorbed into the parameterization by having the other parameters expressed on a daily scale and setting $\delta t = 1$, giving the daily transmission rate. Discretization of eq. 4.7 gives the probability of infection moving from i to j each time step δt

$$p_{ij} = 1 - e^{-\lambda_{ij}}. \quad (4.8)$$

The basic reproduction ratio of the infection, R_0 , is the expected number of secondary cases during the entire infectious period of a newly infected individual (Diekmann et al., 1990). Denoting R_0 of farm i as R_i and following the methodology of Tildesley and Keeling (2009), R_0 is used in Paper III as a premises-level indicator of outbreak risk

$$R_i = \sum_{j \neq i} 1 - e^{-\lambda_{ij} \tau} \quad (4.9)$$

where τ is the infectious period in days for the kernel of choice.

4.2.3 Computational efficiency and gridding

Given the daily infection probability, the simplest approach to simulate infection throughout a population of premises is to calculate p_{ij} for each and every unique pair of infectious and susceptible premises i and j and generate a random number r from $[0,1]$ each daily time step. If $r < p_{ij}$ the susceptible premises will become infected, otherwise it stays susceptible. In practice, this pairwise approach works for small populations of premises but the time complexity of this algorithm grows quickly as the number of premises increases, so more efficient approaches are needed. Two methods are introduced in Paper

Figure 4.2: Illustration of a premises population with two types of grid overlays, regular (A) and adaptive (B).

IV that utilizes a grid structure overlaid on top of the population of premises so that each premises belong to a square cell in this grid (Fig. 4.2). This allows the transmission process to be conceptually layered into two parts, (1) does transmission occur to one or more premises within the grid-cell, (2) if yes, which premises would be inflicted? Given that most farms are distant, the answer to the first part will relatively often be no, and if that step is comparatively cheap computationally, then a lot of time can be saved. Both methods are based on calculating a worst-case probability that infection is transmitted to a premises within the cell. This worst-case probability will always be an over-estimation of any individual true probability that a premises in the cell becomes infected and will stay unchanged during the course of the outbreak. The idea is that if transmission can be determined to not even enter the cell under these exaggerated conditions, it would not be able to infect any of the premises under regular conditions during the given time-step.

The most straightforward simple method to create the grid is to overlay the landscape with equally sized square cells (Fig. 4.2, panel A). However, this leads to large heterogeneity in the number of premises assigned to each grid cell. In densely populated areas, cells will contain many farms while in more sparsely populated areas cells will contain few. This leads to the situation that the over-estimated probability that infection enters a densely populated cell is so large that it will almost always happen. On the other hand, some less populated cells could likely contain more premises and still have a very low probability of getting infection introduced. For these two extreme cases the improved computation method of Paper IV becomes less efficient and starts to work more similarly to the naive pairwise approach. However, by using an adaptive grid creation method where a cell has a target number of member

Landscape	N premises
Random, uniform	208129
Random, low clustering	208129
Random, high clustering	208129
USA, FLAPS	832514
Sweden	24275
UK	177855

Table 4.1: Number of premises in landscapes used in Paper IV.

premises, a set of grid cells that are approximately homogeneous with regard to number of premises can be identified (Fig. 4.2, panel B). A way to find the number of premises per grid cell that is optimal for computational speed is described in Paper IV in addition to the method of simulating outbreaks efficiently within a gridded landscape.

4.2.4 Real and synthetic farm populations

The analysis of Paper III used only the US cattle premises population as generated by the Farm Location and Agricultural Production Simulator (FLAPS; Burdett et al. 2015) consisting of the 48 contiguous states of mainland US. The FLAPS uses a set of predictor variables such as climate, land-use and roads to create a probability density surface of farm locations. Using this probability surface, realistic spatial distributions of the US farm population can be generated. Each realization generated by FLAPS is slightly different owing to the stochastic process of generating locations from a probability surface and ten such realizations with an average of 172,686,644 cattle on an average of 812,703 premises were used in Paper III. For Paper IV, the actual spatial distributions of the premises populations of Sweden and UK were used in addition to one FLAPS realization for the US, and three completely synthetic random landscapes with different degree of spatial aggregation (Table 4.1) created with the method of Lindström, Håkansson, et al. (2011).

4.2.5 Spatial clustering

In Paper III the spatial clustering of the different US counties was used to analyze epidemic risks. We quantified clustering by Ripley’s K (Ripley, 1976), which is a landscape-level measure of how spatially aggregated a landscape is at different radii r ,

$$K(r) = \eta^{-1} \sum_i \left[N^{-1} \sum_{j \neq i} I(d_{ij} < r) \right]. \quad (4.10)$$

Here i and j are premises in the landscape with N total premises, I is a function that evaluates to one if the distance between the premises d_{ij} is shorter

than r and η is the spatial density of premises over the entire landscape. The measure can be interpreted as the premises-level proportion of premises that lie within r , averaged over the entire premises population and scaled by the landscape area. For the county-level clustering, a modified version of Ripley's K was used

$$K_w(r) = \eta^{-1} N_w^{-1} \sum_{i \in w} \left[N^{-1} \sum_{j \neq i} I(d_{ij} < r) \right], \quad (4.11)$$

which describes the contribution of each county w to the landscape-level K .

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