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Existing and potential use of models in the control and prevention of disease emergencies affecting aquatic animals

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Summary

Models are tools that aid managers to make decisions in a transparent manner. Models are implicitly used to devise any management plan, but scientific modelling makes the approach explicit and transparent. Simple models are often more useful than complex models, especially when time and data are short – as in many emergency situations. Four areas in which modelling can help aquatic animal health managers to control or prevent disease emergencies are identified, and their application reviewed. These areas are: models of factors behind disease outbreaks; models for the design of efficient surveillance; models of disease spread (subdivided into Susceptible-Infected-Removed [SIR] models, coupled hydrodynamic-particle transport models and network models); and models to evaluate the consequences of disease outbreaks. Import risk analysis and SIR modelling have been applied fairly extensively; risk-based surveillance is likely to be a driver for increased modelling effort in the near future.

Keywords

Coupled model – Disease emergency – Epidemiology – Network – Risk – Simple model.

Introduction

Disease emergency situations require managers to make decisions – often tough ones – in order to control, mitigate, or, ideally, prevent the problem. These decisions may have to be made quickly and usually with incomplete information. As outcomes may be of great public interest, decision-making needs to be as transparent as possible.

Explicitly or implicitly, all decision-makers use models to derive their expectation as to the responses of a system to proposed interventions. This expectation may just be based on 'gut-feeling' about how the system behaves. Scientific modelling aims to make what is in effect an implicit, opaque and subjective model into an explicit, transparent and objective one. As a model is developed, the assumptions and limitations behind decision-making are made apparent. These assumptions and limitations are NOT created by the modelling process; rather, 'unknown unknowns' are turned into 'known unknowns' that once identified can hopefully be turned into 'known knowns'. It is also likely that decision-makers have experience they have not codified ('unknown knowns' perhaps?); modelling may help expose this hidden knowledge, allowing it to be made explicit for analysis and transparent decision making. However, it is because no model can incorporate all this hidden knowledge that managers must use their judgement in interpreting model results.

The process of building a model forces the key components of a system to be explicitly identified and defined. These components can be considered both in isolation, so their functional nature can be explored in detail (reductionism), and in combination, to analyse their impacts on the overall system (holism). The model building process itself may be the most important outcome of modelling; those participating in the model's construction must develop agreement on the basic structure of the system, or at least come to understand precisely what issues they disagree about.

A basic model can be conceptual, an idea as to how a system fits together; this can be represented by a diagram. With more information, the system's processes and variables (generally lines and boxes in the diagram) may be described qualitatively or quantitatively. Quantitative modelling may be based on simple constant relationships between variables, or complex equations may be used to represent interrelationships of variables and external forcing (38). Models may be deterministic, so repeated runs for a specific scenario give the same results (63). Alternatively, models may be stochastic, incorporating random variation in parameters and forcing that reflects uncertainty, or true variation, in their values; this approach results in a range of model outputs even under a single scenario (74).

As models become more complex, they can be used to make more detailed predictions about more specific events. These predictions allow more extensive testing of the model against observations, if available, and, if this validation is successful, more detail for management. However, additional complexities require additional parameters, and interacting uncertainties as to the values of these parameters lead to uncertainty in the model's outcome (Fig. 1). The number of parameter combinations increases explosively and so exhaustive testing soon becomes impossible. There are T^P combinations (T = number of tests and P = number of parameters); a ten parameter model tested using very low, low, median, high and very high parameter values would require 5^{10}, or nearly 10 million, tests. Therefore, additional complexity is likely to lead to increased uncertainty in the predictions of the model, unless the additional parameters can be strongly constrained by data. Optimising this trade-off between detail and uncertainty is the basic art of modelling (38).

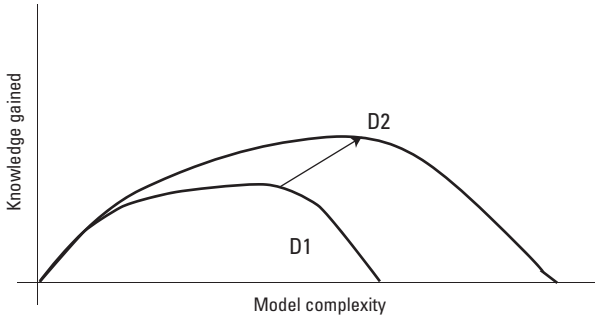

Fig. 1
Model complexity versus the knowledge generated by models
(after Jorgensen, 38)
Line D1 represents the case for basic knowledge while D2 represents the case when more or better quality data are available and more complex modelling may be optimal

Available data, and time to test the model against this data, are likely to be particularly limited during an emergency situation (40). In these circumstances, a series of simple and robust models that capture the basic properties of a system may be used to advise management (3). A complex model, that could give detailed insights, or even drive policy, may be difficult to build and test in the time, and with the data, that is likely to be available.

There are a large number of modelling approaches that are being, or could be, used to help in the control and mitigation of disease emergencies. Here, existing or potential approaches for which modelling can be applied are reviewed under areas for application as follows:

– preventing outbreaks from occurring
– efficient surveillance to allow appropriate intervention
– controlling the spread of disease
– evaluating the consequences of outbreaks.

A final section contains the conclusions of this paper.

Preventing outbreaks from occurring

Prevention is usually the best way to deal with any emergency. In theory there exists an optimal level of risk where the benefits balance the costs of any increased investment in protection (81). However, the benefits in particular may be difficult to quantify (see later section – 'Evaluating the consequences of outbreaks') and so defining an 'acceptable' risk is a management or political issue. The modelling tool most widely used to identify risks of disease outbreaks is import risk analysis, but other methods may include virulence modelling, generalised linear models, Bayesian belief networks and risk mapping.

Risk analysis and exotic pathogens

Risk analysis for diseases of aquatic animals has been extensively reviewed by the World Organisation for Animal Health (OIE) (88). The component of risk analysis that is most relevant here is risk assessment, and specifically the release and exposure assessments; these are the probabilities of the pathogen entering the country or region, and of its coming into contact with susceptible host populations. Risk analysis has been applied to import and to the spread of pathogens from farmed to wild populations (77).

The risk assessment phase starts from a conceptual model diagram describing potential introduction pathways for a

pathogen identified in a previous hazard identification phase. The links in these pathways represent the probabilities of the pathogen transferring between two nodes that represent states of the system. These probabilities can be described qualitatively, e.g. high, low, negligible, but quantitative evaluation may be carried out if there is adequate data and the qualitative results were inadequate for decision-making (106). The probability of infection travelling down a particular pathway is the product of the probabilities of all the links. Uncertainty may be reflected by allowing stochastic variation in probabilities of the edges, and a variety of statistical distributions can be used (e.g. normal, negative binomial). Risk assessment can therefore involve development of quite complex models (e.g. 77). Risk assessment should include assessment of potential consequences, but this is often inadequate (82); consequence assessment is extremely complex (see later section – 'Evaluating the consequences of outbreaks') and data is often lacking, especially for exotic pathogens.

A review of the published application of risk analysis to aquatic animal health (82) found that most were undertaken by developed countries and involved salmonid diseases. However, there appears to be no reason in principle why this method could not be more widely applied. Given the extensive existing literature (88, 100, 106), the application of risk analysis will not be described in any more detail here.

Disease emergence and novel pathogens

Diseases may emerge or re-emerge as pathogens evolve in response to new opportunities and challenges from anthropogenic environmental stresses (71). Evolution of increased virulence in response to increased host availability can be modelled under the assumption of a trade-off between virulence and transmission (10, 22), whereby increased pathogen release results in greater likelihood that the existing host will be killed or injured. If suitable hosts are likely to be in the vicinity, as under dense cultivated populations, a virulent pathogen will spread; if hosts are scarce then less damaging pathogens may have an advantage. Competition between pathogen strains will be likely to select for the more virulent strain (22); this is an example of the ecological principle known as 'the tragedy of the commons', a situation where no party has an interest in conserving a shared resource if others do not.

Different levels of transmission may exist in a population, such that selection for virulence may occur at the farm-level, but if mixing between farms is low (biosecurity to separate farms, fallowing to separate generations) then virulent pathogens may not survive to transmit between populations.

Old pathogens may re-emerge by developing resistance to antibiotics or other medicines. Resistance evolution has been modelled extensively for terrestrial pathogens or pests (14, 51). One model, the high-dose and refuge model, indicates resistance may be avoided if some host populations are given high treatment doses, while other populations are untreated (47). Because more pathogens survive to reproduce on untreated than on treated hosts then, if infection transmits easily between host populations, selection for resistance can be avoided. If all populations are treated, or inter-population transmission is weak, then selection for resistance will be strong. Sea lice have evolved resistance to several treatments (37, 103). Excessive reliance on one medication can create a potentially dangerous situation whose amelioration could be explored using modelling; this might include protection of wild salmonid populations as a refuge.

Disease outbreaks and environmental factors

Disease results from interaction of host, pathogen, and environment (2); following Snieszko (95) this interaction is often visualised using a very simple conceptual model of three overlapping circles (Fig. 2). This model illustrates how fish exposed to pathogens may avoid disease, or perhaps even infection, if the environment is of high quality – good husbandry can reduce the risk of disease emergencies, even if infection is not avoided.

A classical epidemiological approach to identifying and quantifying environmental risk factors is the use of a case-control study to identify odds ratios and build generalised linear models of the associated risk factors. This approach has been applied to disease outbreaks among farmed salmonids (34, 35, 36) and shrimp (12, 48). An alternative approach that also uses large amounts of data to identify risk factors is the use of neural networks, which have been used on diseases of farmed shrimp (48). Both approaches require considerable quantities of data, and so are unlikely

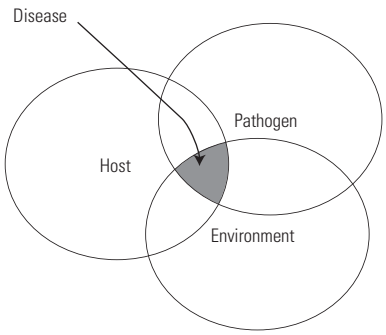

Fig. 2
Three circles conceptual model of disease (after Snieszko, 95)
Only in the shaded area where the pathogen, host suitability, and poor environment coincide will disease occur

to be applicable from scratch in an emergency situation. Risk factors identified from earlier studies may be very useful to protect against exotic disease or to protect individual farms from outbreaks of endemic disease. Causality for any associations found between risk factors and disease is not determined, so there is uncertainty in the applicability of these risk factors to new situations.

Risk analysis has been used to identify general mechanisms behind disease emergence (71). This analysis was based on the identification of risk factors behind a pathogen's emergence or introduction, its ability to spread between and within populations, and the consequence should this happen.

Bayesian belief networks could be used to analyse the interactions of risk-factors behind disease outbreaks. Here, the overall probability of an event is determined by networks of interacting variables. Each variable has a finite number of states (e.g. low, medium or high), whose respective conditional probabilities depend on the state(s) of the variable or variables that link into them. If rainfall was 'high' the probability of local salinity being 'high' might, for example, be 5%, but had rainfall been 'low' this probability might be 90%; pathogen levels might, in turn, depend on salinity. Belief networks use explicit descriptions of how a system is believed to work and so can identify mechanisms behind disease outbreaks. They can be useful for incorporating non-scientific knowledge into a scientific or management framework. This approach does not appear to have been used to study outbreaks of pathogens affecting aquaculture, but it has been applied to identifying environmental factors associated with the decline of trout populations (6) and likely changes in coral reef bleaching in response to global warming (112).

Risk mapping can be used to identify low or high risk environments if risk factors are geographically distributed. Habitat suitable for disease-carrying ticks has been mapped in this way (30). Risk from fish diseases with intermediate hosts might be mapped using the habitat of these intermediate hosts. For example, cryptocotyle infection in farmed cod (28) might be avoided using risk maps based on the rocky shoreline habitat of the intermediate periwinkle host.

Efficient surveillance to allow appropriate intervention

Minimising the spread of an invading pathogen depends upon rapid response by managers and officials. This rapid response requires rapid detection and reporting of the presence of pathogens; detectability of a pathogen can be as important as its inherent rate of spread (R_0) for disease control measures (23). Data on the presence of pathogens may be available from many sources in addition to official disease surveillance services (58).

The aim of surveillance is likely to be minimising the chance of pathogen spread before it is detected, but it may be to assess a pathogen's prevalence or to provide a strong assurance that specific sites are disease-free. These aims require different surveillance strategies and so the purpose of surveillance must be made explicit. Recent interest in risk-based surveillance (96) has brought more attention to risk factors as the focus for surveillance. Sites at risk of receiving or spreading infection can be identified using modelling methods such as import risk analysis, Susceptible-Infected-Removed (SIR) modelling, hydrodynamic modelling and contact-structure modelling, which are described elsewhere in this paper. Cost-benefit analysis has been used to assess whether a surveillance programme represents an effective use of resources (61). Surveillance of slaughterhouses might be a cheap and effective way of demonstrating that a country was disease-free, however, if an introduction did occur the pathogen might spread throughout the industry before it were detected if this were the only stage sampled.

Simple statistical modelling can precisely assess the effectiveness of sampling regimes, for a given pathogen distribution and a specified aim for the surveillance. Consider a case where one of ten farms is infected at 1% prevalence and 300 fish may be sampled. In the absence of specific information it would be better to take 30 fish samples from each farm (30% chance of detection) than 300 samples from 1 farm (<10% chance of detection), as there is a 90% chance the infection was on one of the other nine farms; however, the latter approach would be appropriate if the desire was to ensure specific sites were free. Under risk-based surveillance, sampling would concentrate on high-risk farms, which would be likely to include the infected farm; if available intelligence were perfect, then sampling entirely at the infected farm would give a 95% probability of detecting the pathogen – but if intelligence were poor the result could be the 10% probability found under random sampling of a farm (or worse if the intelligence were actively misleading). Thus, the same level of sampling could give 10%, 30% or 95% probability of detection.

If the aim of surveillance is to quantify variation between sub-populations then sufficient fish must be taken in each individual sub-sample for these sub-samples to be quantified (93). However, the population level of interest must be clear, for example, to quantify sea lice prevalence at the farm-level it is better to sample a few fish from many cages rather than many fish from a few (86). Such sampling does not allow cage-level prevalence to be evaluated; but such information is not needed to estimate

farm-level production of lice eggs, which is the avowed aim of this surveillance.

Sampling to quantify macroparasites may be complicated by the variation of loads between individual infected hosts. As parasites are generally not normally distributed among hosts, a few hosts with high loads may have a big effect on mean sample load (111). Even the distribution of parasites on a single host may affect the optimal sampling regime, for example, fin sampling for *Gyrodactylus salaris* will be less effective than whole-fish sampling if the aim is to accurately quantify prevalence or intensity. However, if more fins than whole fish can be sampled then fin sampling may increase the probability of detecting the presence of *G. salaris*, depending on distribution on and off the fins. The relative benefits of fin sampling could be determined from observational data (29) and simple statistical models of the probability of parasites being present on fins.

Real tests are not 100% sensitive and specific, this means false positive results can emerge. Bayesian methods can be used to estimate predictive powers of tests, by estimating the ratio of false positive to true positive (and false negative to true negative) using sensitivity and specificity and population prevalence (58). For example, positive predictive power is:

$$PPV = SeP/(SeP + (1- Sp)(1 - P))$$

Where P = prevalence, Se = sensitivity and Sp = specificity. If P is small and/or Sp is low, PPV becomes low and so a positive result is relatively likely to be a false positive. Predictive power could be extremely useful for informing managers' response to test results, but in practice is rarely explicitly considered.

Estimates of sensitivity and specificity can be made using Bayesian statistical models. These methods involve comparing the prevalence obtained by two or more tests from two or more populations with different infection prevalences to estimate levels of false positives and false negatives (73, 84).

Many more data are collected about disease than just those from official structured surveillance. These data can be used to strengthen proof that a country is free of a specific disease, but objectively using such data (of variable value) has been difficult. Martin *et al.* (58) describe the use of scenario tree modelling (Fig. 3) to bring in different sources of data into an overall estimate of the power of a national surveillance system. This promises to be a powerful technique to incorporate many sources of data on fish health that are not effectively used currently. Building trees breaks down the complex problem of the effectiveness of surveillance into simpler steps and makes explicit the relationships between different components.

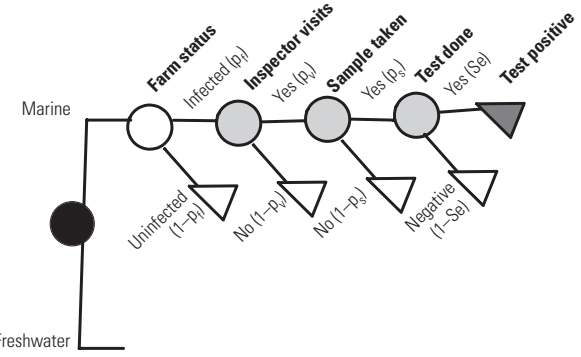

Fig. 3
Simple scenario tree model for the probability of detecting a disease in farmed anadromous fish (Martin *et al.,* 58)
The probability of detecting disease at the industry level is marked by the black circle, this derives from the combined probabilities that infection will be detected in any individual farm. For each individual marine farm (open circle) the probability that infection will be detected is the product of $p_f \times p_v \times p_s \times Se$ (i.e. the probabilities that the farm is infected, that it is visited by inspectors, that a sample is taken, and that the test used is sufficiently sensitive; these steps are marked by grey circles). Detection at the farm level is marked by a grey triangle, while the white triangles show outcomes whereby infection is not detected at the farm level. A similar path, the details of which have not been included in this figure, exists for freshwater farms, although p values may be different at each step. Trees can be derived for other forms of surveillance and combined to give the total probability of detection

Analysis of the resultant trees may indicate changes to the allocation of resources that would strengthen surveillance power – another tool for developing risk-based surveillance.

Efficient sampling that is well designed for its purpose can assure with high probability that a country or other area is disease-free, and ensure rapid detection should a pathogen emerge. Statistical modelling is a powerful tool for objectively designing efficient sampling with respect to a specific objective and assumptions as to pathogen distribution. Free software is available at sites such as www.ausvet.com.au for test sizes for demonstrating disease freedom and www.epi.ucdavis.edu for determination of sensitivity and specificity of tests.

In spite of these well-described methods, inefficient sampling methods are often used in practice, such as concentrating sampling on a few cages at a farm or using small samples to declare sites as free from low-prevalence pathogens. Monitoring practices are often conservative, and new surveillance regimes are often based on old ones, rather than designed from scratch; legalistic fulfilment of required sampling also induces conservatism. Application of risk-based surveillance may increase the use of epidemiology in explicit evaluation of schemes.

Controlling the spread of disease

If a pathogen does enter a new region or compartment, then understanding the factors behind its spread is essential if controls are to be developed (100). Three approaches are examined: traditional epidemiological SIR-type modelling, hydrodynamic modelling of pathogen dispersal, and network modelling.

Susceptible-Infected-Removed models

Basic principles

Traditional epidemiological modelling (1, 85) is based on the SIR concept (Fig. 4). Similar approaches apply to larger parasites, although complexities arise because individual hosts have different parasite loads (60). The susceptible population (S) is the part that has not yet been infected, but may become so by interacting with those that are already infected (I). This infected phase may be split into incubating and infectious phases in some models. The removed phase (R) is not part of the epidemic; depending on the disease, R individuals are either immune and recovered, or dead. Populations may consist of individuals or of sub-populations, such as farms in a region. Underlying principles must be considered when applying models derived for terrestrial systems (56); however, simple models do allow the basic factors behind the spread of the epidemic to be examined.

The simplest form of such models is:

$dS/dt = -bIS$
$dI/dt = bIS - mI$
$dR/dt = mI$

Under this formulation the rate of formation of new infection is bIS, while the rate of recovery (or death) is mI; parameter b is the transmission coefficient and m is the recovery or mortality rate. This simple form can be applied to short-lived epidemics, where factors such as births and non-disease mortality are not significant (69).

Fig. 4
The Susceptible-Infected-Removed model structure (1)
The host population is divided into susceptible (S), infected (I) and removed (R) categories and infection is transmitted from I to S by some function of interaction, typically bIS, i.e. transmission is proportional to the populations of susceptible and infected hosts

As an example, suppose an infected host infects 2 individuals per day in a naïve population, and recovers after 1 day, then b = 2 and m = 1. In the naïve population S is close to 1, but because I is small there are few sources of infection so the epidemic spreads slowly. As I rises the infection initially spreads more rapidly, although the rate-per-I drops. As susceptible individuals become rarer so infection rate, and eventually I itself, declines (Fig. 5).

Pathogens spread if the rate of formation of new infections is greater than the rate of recovery, or death, of infected hosts (or populations). This can be mathematically described using an increase ratio R_0 that is derived by dividing the rate of creation of new infections by the rate of removal (recovery or death) of infected hosts (85). If $R_0 > 1$ an epidemic can result. Under the simple model above, the increase ratio is $R_0 = bS/m$ (= 2×1/1 = 2 for the example parameters above in a naïve population where S = 1). A minimum threshold population density of S that is required for an epidemic can also be derived as $S_t = b/m$ (= 0.5 for the example parameters). The formulae of S_t and R_0 depend on the epidemiology of a particular disease, especially the mode of transmission of infection (55, 85).

The simple model shows how disease might respond to interventions which reduced transmission ([b] improved biosecurity) or increased removal of infection ([m] treating or culling of infected hosts, removal of moribund fish). In the simple density-dependent model used here, reducing the susceptible population S is also effective, although this may not be the case for density-independent diseases (1, 69).

The SIR models can also be used to analyse dynamics of infection (Fig. 5), including calculating the total size of an

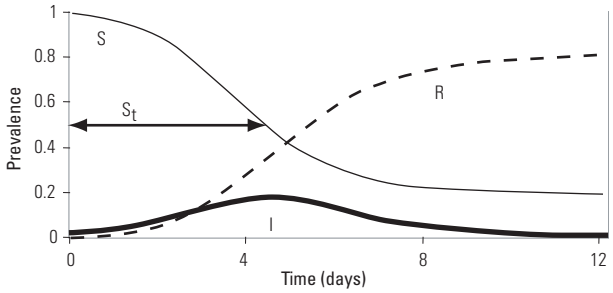

Fig. 5
An example of an epidemic simulated using a Susceptible-Infected-Removed model
Initially the population is nearly 100% susceptible, S (thin line), with a few infected individuals, I (thick line). Infection spreads rapidly, but as available S declines so does infection rate. Eventually the infection threshold S_t (double arrow) is reached ($R_0 < 1$) where creation of new infection is balanced by recovery or deaths (to R, dashed line) and so I start to decline. Final disappearance of the epidemic may take a considerable time and S continues to decline during this period

epidemic and its likely duration. Transient responses to interventions reducing R_0, perhaps only temporarily, can be explored in this model.

One implication of the density-dependent transmission model is that disease might reduce in some over-exploited populations (18); there is some evidence that diseases may have reduced in overexploited fish and increased in their predation-released prey (45). Fishing can also reduce disease impact by removing infected hosts, as has been simulated for a crab fishery (44). In a disease emergency the pre-emptive fishing out of wild stocks might be a usable tool to reduce the impacts of an epidemic by either reducing total mortality or at least maximising usable catch (41, 62).

SIR modelling has been used to analyse the interaction of pollution with disease (49). This interaction is complicated because under contamination more rapid mortality of infected animals and lower population densities may reduce pathogen prevalence, while increased susceptibility to infection may increase its prevalence.

Models of specific diseases

The SIR modelling approach has been used to develop more detailed models of specific diseases. However, greater model detail requires more data and testing, so such models may only be practicable after the event, and hence not used to guide interventions.

Farm-level outbreaks have been modelled for microparasite diseases, including the shrimp diseases white spot syndrome (WSS) (54), Taura syndrome (53) and necrotising hepatopancreatitis (105); in the models for these diseases cannibalism of dead shrimps plays a major role in disease spread. Single population SIR models have also been developed for infectious pancreatic necrosis (IPN) (94) and furunculosis (74, 75, 76) using data from experimentally infected populations. Transmission between different ponds within a farm has also been simulated for general disease spread (113). Stochastic variation in epidemic development has recently been included in a model of furunculosis epidemics, allowing the variation in potential epidemic development to be simulated (74). These models have potential for developing effective within-farm intervention, but for the moment remain research tools rather than directing practical interventions in the face of an outbreak. Such models may have the potential to be useful for planning active interventions, e.g. optimising antibiotic treatments; identifying specific applications requires a collaboration of epidemiologists and farm managers.

Dynamic models of diseases in single wild populations have also been developed to describe lymphocytosis in flounder (52), parasitic castrators in crabs (44), and diseases in oysters (21, 33, 41). These are endemic diseases and do not represent emergency situations, although management to reduce impacts may be practicable (44). These models may also predict the impact on disease distribution of factors such as climate change (33).

Models of the spread of macroparasites in single populations, such as farms, have the potential to be usefully applied in preventing or moderating future outbreaks. Examples are models of sea lice outbreaks at the farm, or single population, level (87, 97, 104), which provide predictions as to treatment intervention effectiveness with respect to parasite development stage. A model of the freshwater parasite *Argulus*, also at the farm-level, provides predictions on the effects of egg banks on treatment strategies (19).

SIR models of various levels of complexity were applied to geographical spread of pilchard herpesvirus (PHV) in Australia (68). A relatively simple model was developed that allowed a fairly rapid analysis of the basic processes behind epidemic spread (69). Numerous copies of the model were implemented to represent local pilchard populations along the Australian coast. Neighbouring populations interacted using a diffusion equation to determine rate of transfer of infection (68); this resulted in infection spreading along the coast as a wave of constant velocity. A more sophisticated version of the model allowed accurate simulation of observed wave shape as well as speed (70), which allowed detailed analysis of the relative roles of local and long-distance transmission. Long-distance transmission was shown to be consistent with movements of fish, rather than birds or anthropogenic vectors. Pilchard herpesvirus may have become endemic in Australia since the 1998/1999 epidemic (110), if so, these epidemics are unlikely to be repeated, but the models might be relatively quickly adapted to analyse controls for other diseases that are spread by similar means.

Geographic spread of phocine distemper virus (PDV) around the North Sea and adjacent areas resulted in mass mortality of seals in 1998 and in 2002 (26). The spread of this disease has been modelled in detail (99). Spread was due to interaction of susceptible and infected seals in 'haulouts', such as sandbanks, where seals congregate. The North Sea seal population was divided into sub-populations representing the seals using each haulout. Long-distance spread of waves of infection was due to relatively small numbers of seals that moved between haulouts.

Spread among salmon farms of IPN virus (IPNV) has been modelled using Scottish fish health inspectors' data and a Susceptible-Infected approach (63). Farms were classed as I if any infected fish were present, otherwise they were classed as S (Fig. 6). An R class was not included as infection was not lost, at least at the population level, until

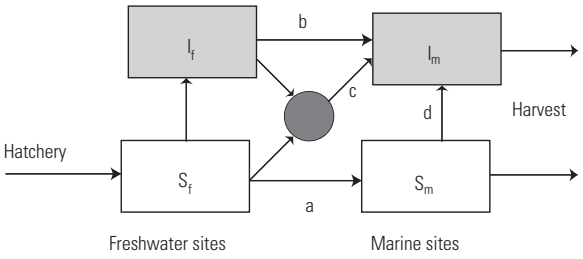

Fig. 6
Susceptible-Infected model structure as applied to simulate the spread of infectious pancreatic necrosis virus in Scotland and Ireland
The model consists of freshwater and marine phases. Fish enter the freshwater phase as infection-free fry but may pick up infection. Fish are transferred to sea water carrying infection, and sites that use multiple sources of smolts become infected if some (b) or all (c) of their sources are infected. If they avoid infection from freshwater sources (a), the fish may still become infected (d) while at sea. Infection persists until harvest

harvest. The population was divided into freshwater and marine phases, and marine farms could accept smolts from several freshwater sites, multiplying their risk of infection. The virus' spread was simulated at the national Scottish level and at various regional levels. The top population level simulated was treated as well mixed, but no mixing was included between regions when these were simulated individually, some regional-level simulations poorly matched observations, indicating that inter-regional movements played a significant role in the epidemic.

Because IPNV in Scotland took several years to change from low-prevalence to becoming almost ubiquitous, it was possible to develop and test the model, and to make predictions of the future course of the spread, and its response to quite detailed interventions, while this spread was still occurring (63). However, even in this case, it was only possible to obtain enough data to make predictions once the virus was well established and so these predictions were largely that controls at that stage were unlikely to be effective or cost-effective. The model has been applied to an earlier stage of spread of IPNV in Ireland (Ruane *et al.*, in prep., 90) and expanded to include potential effects of international trade.

Simple SIR models are a very useful means of analysing dynamics of infections and basic responses to controls. More detailed models of individual diseases are also providing tools for analysing controls on outbreaks at the farm level or for repeated or slow spreading outbreaks on larger scales; however, such models take time to develop and so the simpler models are likely to be more useful for a novel outbreak.

Hydrodynamics

Aquaculture takes place in water, a literally fluid environment (Fig. 7). This may be of great importance for the patterns of pathogen exposure of hosts. Those hosts at greatest risk of infection may be distant from the existing infected population.

Modelling demonstrates how farming can increase infection pressure in the coastal zone as a whole (31), potentially endangering populations not previously exposed such as juvenile salmon (42). Hydrodynamic flows will determine where, or if, any risk manifests itself.

Coupled hydrodynamic-particle modelling takes a hydrodynamic model that calculates water flows and a model that simulates the properties of dissolved or suspended particles. This approach is used to simulate distribution of objects and substances, such as planktonic larvae (5), transported by water movements.

Hydrodynamic models are complex and can take considerable effort to develop and validate, and considerable computational run time. The currents generated by hydrodynamic models are not dependent on the particles they transport and so can be developed without specifying the pathogen transported. Hydrodynamic models can thus be developed prior to a disease outbreak, quite possibly for some completely different purpose. A single hydrodynamic scenario can be used to drive many biological scenarios, and so a relatively small number of runs may be required.

The particle-tracking model calculates the motion of particles using current velocities generated by the hydrodynamic model. The particle-tracking model also

Fig. 7
A buoy deployed to record currents in Loch Torridon (in the North West Highlands of Scotland) as part of a cross-cutting Fisheries Research Services (a Scottish government agency) oceanographic and biological study of larval sea lice transport

simulates decay or transformation of non-conservative particles, e.g. decay of viruses exposed to ultraviolet (UV) light by water movement (67) or maturation of sea lice, from harmless nauplii to infectious copepodids (66). This requires biological information on the properties of the particles, and so different diseases must be simulated separately. Due to uncertainty or variability in the value of biological parameters, it may be necessary to repeatedly run the particle-tracking model (for a particular hydrodynamic model scenario) with different values and so obtain a range of results. The outcome of this process is a prediction of areas exposed to high concentrations of pathogens (Fig. 8). Simple versions of this approach have proven useful in developing tools for tackling emergencies. For example, eradication of infectious salmon anaemia (ISA) from Scotland was achieved partly through the development of surveillance zones based on a simple model of pathogen dispersal that assumed virus was dispersed for one tidal excursion distance (64). Sites whose tidal excursion zones overlapped formed a surveillance zone which was lifted when the last site in the zone had been fallowed. This model required no biological modelling of the ISA virus (ISAV) particles, and hydrodynamics were restricted to a simple sinusoidal current whose excursion distance was dependent on maximum tidal velocity.

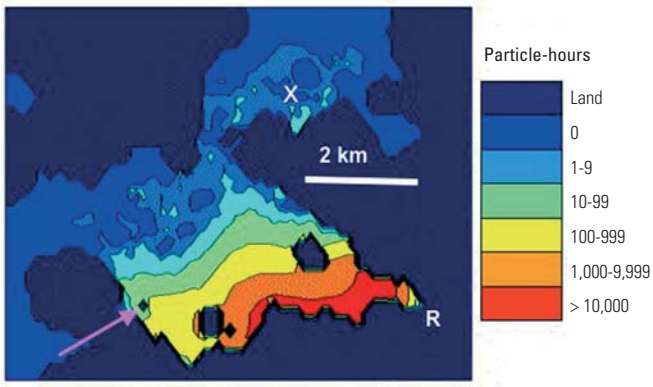

Fig. 8
Example sea lice dispersal scenarios from the Loch Torridon model
Map shows distribution of relative risk of infection (in log units) from lice released at the location marked by the pink arrow, risk is described in terms of 'particle-hours' (the number of hours that simulated particles are present in each model grid square), e.g. 10 particle-hours could be due to 1 particle present for 10 hours, or 10 particles for 1 hour. Two populations potentially at risk of infection in this area include the sea trout population of the Shieldaig River (R) and the salmon farm in Upper Loch Torridon (X)

A slightly more sophisticated model involved sinusoidal tidal advection, constant non-tidal advection, and turbulent diffusion. This model was combined with a simple particle shedding and decay model to simulate dispersal of ISAV, IPNV and sea lice; sea lice larvae were modelled as having a fixed life-span rather than a decay rate (64). Simulations indicated that labile ISAV was unlikely to travel beyond the tidal excursion zone at biologically significant concentrations, hence supporting the simple approach that had been used to devise surveillance zones. However, more refractory IPNV and sea lice were likely to be transported to locations outside the tidal excursion zone, indicating that more sophisticated hydrodynamic modelling was required.

Physically close sites that are not connected by currents might be placed in separate control zones if these could be derived with confidence using detailed hydrodynamic models. Infectious salmon anaemia infection is biased to down-stream sites (25). Similarly, dispersal of infectious haematopoietic necrosis virus (IHNV) reflects net flows in British Columbian water (98). It is in the area of sea lice where the roles of hydrodynamics and biology in generating infectious particle distributions (Fig. 8) have been modelled in most detail (4, 8, 24, 66), although sea lice have also been modelled assuming distribution is centred on infested farms (43).

Complex coupled models would be difficult to generate during an outbreak. Simple models have proven useful in the control of ISA in the face of a serious emergency. More detailed models may be useful for tackling ongoing (sea lice) or repeated infectious haematopoietic necrosis (IHN) problems. Because hydrodynamic models can be developed without reference to the specific particles transported, these could be prepared prior to a specific disease issue arising. However, the coupled particle model must incorporate biology; this is specific to the pathogen and may be complex, especially if the pathogen (e.g. larval sea lice) has some mobility.

Networks

Patterns in spread of disease outbreaks can be very different if infectious contacts are only between neighbouring populations or occur through long-distance (usually anthropogenic) movements (Fig. 9). Even when such long-distance events are rare they can have a disproportionate impact on an epidemic, as illustrated by the 2001 foot and mouth disease epidemic in the United Kingdom, during which a small number of long-distance movements set up a number of separate local epidemics, each of which caused many local cases (39). It is therefore of great practical value to interrupt such long-distance transmission and since the movements are usually anthropogenic this is, in principle, possible.

Simple networks have been simulated as a circle of nodes (108) which at one extreme only interact with their neighbours, at the other extreme they interact randomly

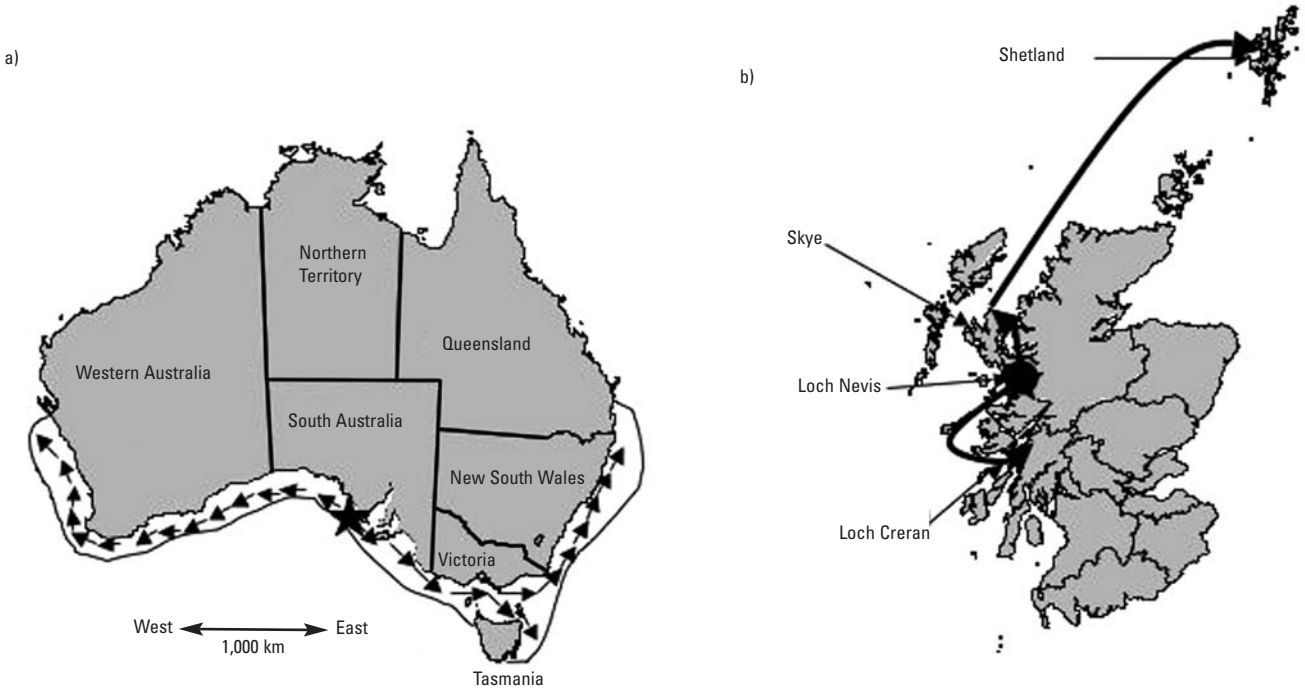

Fig. 9
Examples of two different patterns of disease spread
(a) Pilchard herpesvirus infection in Australia spread as a wave of constant velocity through the wild population
(b) Infectious salmon anaemia in Scotland spread as disjointed outbreaks associated with movements of fish- and harvest-transporting well-boats between farms

with other nodes no matter how distant they are on the circle (Fig. 10). A disease will take a relatively long time to travel through such a network if it is spread only between neighbours, and there may be opportunities to interrupt this spread. If interaction occurs at random, the disease can spread far more rapidly through the system and there are no obvious breaks to prevent this spread, although general controls on long-distance movements may well be possible. A small number of such random interactions can greatly accelerate a disease's potential rate of spread (Fig. 10).

Network structure becomes more complex if the nodes are not uniform. Some nodes rarely interact with others (e.g. the only large movement off many on-growing marine salmon farms is likely to be for slaughter), others interact very frequently (e.g. hatcheries have many movements of fish to other sites). Infection in an on-growing site quite likely might be a dead-end event, while an infected hatchery can spread disease throughout the country, or beyond. Frequently the number of contacts exhibits a power-law distribution, which means small numbers of sites have many interactions. The probability of ISA outbreaks in Scotland during the epidemic of 1998/1999 was related in a statistical model to the number of visits by well-boats, so sites with many visits were at greater risk (72). Disease may spread in such networks, even if average $R_0 < 1$.

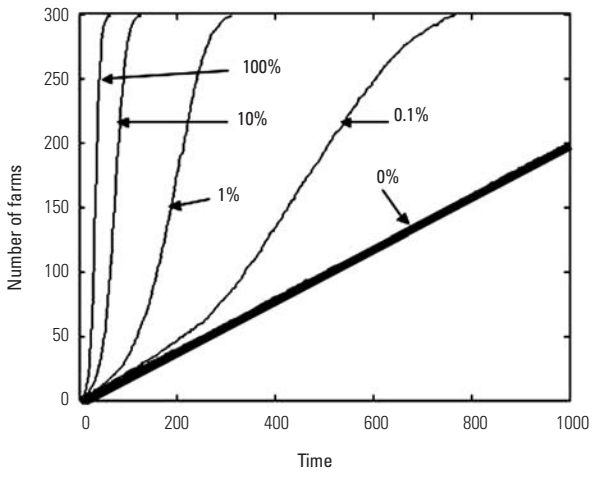

Fig. 10
Time required for infection to spread through a network of 300 sites arranged in a circle and interacting either with immediate neighbours or randomly throughout the network
In this simple model infection is permanent. Random interactions account for 0, 0.1, 1, 10 or 100% of these contacts. Even a small number of random transmission events cause a large increase in rate of spread relative to when transmission is only between neighbours (thick line)

Contact-structures have been used to simulate potential invasions of pathogens in England using a simple model

based on the numbers of movements of fish between catchments (101) and by a more complex model of the interaction of sites, including sites within catchments (92). Such models are largely based on analysis of existing fish movements, and therefore data to build them can be obtained prior to a disease being introduced, and they can be used for emergency planning before specific problems emerge. These models have been used to derive estimates of the potential scale of epidemics of invading pathogens, and variation in this scale.

Conversely, patterns of outbreaks can be used to assess the contact structure of the system. Distance from other outbreaks and shared ownership of sites (a simple measure of membership of a network) has been used to estimate the strength of association of local and network factors with spread of ISA in Norway (91). Such use of outbreak data requires that many cases have already occurred, and so will be of limited use in an emergency.

Simple spatial transmission models correspond to extremes of the contact-structure model. Spread of PHV was simulated only between adjacent populations (68), as was PDV spread between seals in neighbouring 'haulouts' (99); these are equivalent to 0% random contact (Fig. 10). The PHV and PDV models generated waves of mortality that travelled through the populations at constant velocity. The spread of IPNV between farmed populations was simulated without explicit spatial structure, at least within (marine or freshwater) environments (63); this is equivalent to 100% random contact throughout the farm network (Fig. 10). All three models derived inter-population mixing rates from observed disease spread, rather than from analysis of the contact-structures. However, derived mixing rates for PDV and PHV were shown to be consistent with seal (99) or pilchard (69) swimming patterns.

An understanding of network structures is important for the development of risk-based surveillance schemes (96), because highly connected nodes are at greater risk of becoming infected or of spreading infection once infected. Explicit modelling is not generally used to drive surveillance, but features of many surveillance systems, such as increased surveillance of hatcheries, are implicitly based on such assumptions; as we argued in the introduction, making such models explicit would allow their assumptions to be tested, challenged, and refined.

Evaluating the consequences of outbreaks

The management of disease emergencies can be expensive, but failure to manage can be even more costly (32). These consequences may manifest themselves as direct effects on host populations, or indirectly elsewhere in the ecosystem. The cost of these consequences must be balanced against the costs of measures used for risk reduction (61, 81), yet consequence assessment of aquatic disease is often limited or non-existent (82, 100).

Fish population models, as used to derive allowable catch, have been used to estimate disease-induced loss to herring fisheries in the North Sea (79) and North Pacific (59) using observed prevalence of pathogens or symptoms. Patterson (79) estimated up to 9.6% of potential herring fishery production was lost due to the fungus *Ichthyophonus* in the worst-affected years. Murray and Gaughan (65) adapted an existing model of pilchard population dynamics (20) to analyse population recovery following PHV-induced mass-mortality. Impact of disease may depend on the age-classes in a population that are affected; this can be analysed using models (15, 41, 42, 65).

Disease may also have indirect impacts elsewhere in the ecosystem. For example, PHV epidemics caused starvation and recruitment failure of predatory little penguins (13) and increases in the numbers of competing anchovies (107). Models of the impact of mortality of tilapia on piscivorous pelicans have been derived for the inland Salton Sea in California (11). Existing approaches to the modelling of aquatic ecosystems and fish population dynamics are quite advanced (80) and the inclusion of disease impacts in such models may be an important area for future research (78).

Pathogens may compete with other pathogens (89) or act as hyperparasites that may kill other pathogens or parasites (102). Sealworm decline in cod was noted following mass mortality of seals from PDV (16), which was predictable from models of cod's worm burden that was related to seal populations (17).

Financial losses have often been estimated by 'back-of-envelope' approaches in which the production losses are roughly estimated and a cost attributed to those losses. Headline figures can be estimated for the financial impacts of disease outbreaks that have occurred, such as £25 million (US$ 51 million) for the 1998/1999 ISA epidemic in Scotland (27) or very large costs often running into hundreds of millions of dollars for different countries affected by WSS (32). Such rough estimates can also be derived *a priori*, or at the onset of an epidemic, by estimating the value of an industry and making simple assumptions as to the direct and indirect losses a disease might cause. Simple assessment may be very useful in determining a rough appropriate budget for prevention, control or eradication policies.

More sophisticated modelling of economic costs of the impacts of sea lice at the farm-level have been described by

Pike and Wadsworth (83) with cost-per-fish, break-even points and treatment margins to assess the value of lice treatment (81). Such economic models could be combined with epidemiological models of sea lice (86). The break-even model was used to assess the value of vaccination against vibriosis (50). The impact of cardiomyopathy on farmed salmon has also been analysed using a model that combines epidemiology and economics (9). Here the most economically efficient strategy is not the most epidemiologically effective, since it can be worthwhile delaying culling to allow surviving fish to grow to a larger size that fetches a higher price. Costs and benefits of surveillance programmes for ISA, IHN and viral haemorrhagic septicaemia carried out in the United Kingdom have recently been assessed using modelling (61). Existing models assume simple relationships between intervention costs and reduction in disease losses; they do not take into account secondary reduction in infection due to the reduced infection pressure. Economic approaches can give detailed insight into appropriate management of disease outbreaks at the farm level. However, application of detailed economic modelling to larger-scale events is currently limited by the difficulties of detailed epidemiological modelling during an emergency.

Models of the value of aquaculture at community and higher level (57) might also be useful for assessing the wider potential impacts of epidemics, and hence fixing appropriate budgets for their control. Socio-economic modellers acknowledge the need for inclusion of events such as disease outbreaks to increase confidence in their assessments as to aquaculture's long-term sustainability (57).

Estimation of the economic impact of disease is particularly difficult for such issues as conservation of endangered species, environmental protection, welfare protection, or recreational fisheries. Here losses would often not be directly financial, yet any losses would be real and money must be spent to protect against them. Managers, with limited funds, have to assign a financial value to this damage if their expenditure is to be allocated appropriately. Contingency methods use questionnaires in an attempt to assess the amount of money people would be prepared to pay to prevent a specific impact; subtle questioning is required to obtain valid data (109). They have been used to evaluate recreational fisheries (46) and wildlife conservation issues (7), and to estimate potential impacts of exotic diseases (61).

Conclusions

Scientific modelling consists of a range of methods for making our understanding of a system both formal and transparent. The process of model development helps to improve understanding of the system's behaviour and identifies specific areas of lack-of-knowledge or of disagreement. Resultant models are a useful means of predicting how a system is likely to respond to impacts, such as invasion of a disease and mitigating management actions. However, complex models require much data (Fig. 1) and time to validate and as such may be of limited use, especially in an emergency. Simple robust models may be more informative, and should guide, not direct, management action.

The objectives of modelling, and the nature of the systems modelled, must be understood when selecting methods. Many existing disease models were originally developed for terrestrial environments where disease properties, especially transmission, may be qualitatively different from those in the aquatic environment (56, 66). Even where modelling theory is well developed it may not be applied correctly, as appears to be the case with the design of some sampling regimes (86).

In this paper a range of issues benefiting, or that could benefit, from the application of modelling have been identified. Models of import, emergence and environmental risks may be useful for reducing the risk of disease outbreaks occurring. Risk-based surveillance allows limited resources to be applied most efficiently to detect pathogens (provided the risk model is appropriate). Transmission models include a range of SIR-based models from simple general models to more complex specific disease models, models of hydrodynamic transmission of pathogens, and network models. These models can provide powerful insights into the potential, or lack thereof, of different intervention strategies. Consequences of disease outbreaks, including wider ecological and economic effects, can also be assessed using models; an assessment of these consequences (including non-financial) is required when deriving budgets for disease control.

Import risk assessment has to date been the most extensively subject to applied modelling in aquatic disease management. Transmission modelling of the SIR type has been used to describe several diseases and provide information on their dynamics in general and specific cases. This has provided insight, but so far has only had limited value directly in the control of outbreaks (detailed models often being developed only after the event). Perhaps the area where modelling may be expected to see the most rapid increase in application is in the support of the development of risk-based surveillance programmes using established probability theory and new network and scenario tree methods.

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Modèles applicables dans le cadre du contrôle et de la prévention des urgences sanitaires affectant les animaux aquatiques : utilisations concrètes et potentielles

A.G. Murray

Résumé

Les modèles sont des outils permettant aux gestionnaires de prendre des décisions de manière transparente. Si tous les plans de gestion font implicitement appel à des modèles, la modélisation scientifique rend la démarche explicite et transparente. Les modèles simples s'avèrent généralement plus utiles que les modèles complexes, en particulier lorsque l'on dispose de peu d'informations et de délais très brefs, comme c'est le cas dans la plupart des situations d'urgence. Après avoir identifié quatre domaines pour lesquels la modélisation peut aider les gestionnaires de la santé des animaux aquatiques à prévenir et à maîtriser les urgences sanitaires affectant ces animaux, l'auteur examine chacune de ces applications. Il s'agit de la modélisation des facteurs responsables des foyers de maladie ; de modèles pour la conception de plans de surveillance efficaces ; de modèles de diffusion des maladies (subdivisés en modèles « sensibles-infectieux-retirés » [SIR], en modèles couplés hydrodynamiques et de transport de particules, et en modèles de réseaux) ; enfin, de modèles d'évaluation des conséquences des foyers de maladie. À l'heure actuelle, l'analyse du risque à l'importation et les modèles SIR sont assez communément utilisés ; la mise en œuvre de plans de surveillance fondés sur l'analyse du risque devrait inciter à recourir davantage à la modélisation dans un proche avenir.

Mots-clés

Épidémiologie – Modèle couplé – Modèle simple – Réseau – Risque – Urgence sanitaire.

Utilización real o posible de modelos para controlar y prevenir emergencias sanitarias en animales acuáticos

A.G. Murray

Resumen

Los modelos son herramientas que ayudan a las administraciones a adoptar decisiones con transparencia. Aunque de manera implícita forman parte de cualquier plan de gestión, la elaboración de modelos científicamente fundamentados hace que el proceso decisorio resulte más transparente y

explícito. Los modelos sencillos suelen ser más útiles que los complejos, sobre todo cuando hay poco tiempo y faltan datos, circunstancia corriente en muchas situaciones de emergencia. Tras delimitar cuatro ámbitos en los que la elaboración de modelos puede ayudar a los responsables de sanidad de los animales acuáticos a controlar o prevenir enfermedades, el autor pasa revista a la aplicación práctica de este tipo de herramientas. Los mencionados ámbitos son: modelos de los factores subyacentes a los brotes infecciosos; modelos para la concepción de sistemas eficaces de vigilancia; modelos de propagación de enfermedades (que a su vez se subdividen en: modelos con eliminación de ejemplares susceptibles o infectados; modelos combinados de hidrodinámica y transporte de partículas; y modelos de redes); y modelos para determinar las consecuencias de brotes infecciosos. El análisis de riesgos derivados de la importación y los modelos con eliminación de ejemplares susceptibles o infectados son sendas herramientas utilizadas muy a menudo. Es probable que en un futuro próximo la vigilancia basada en la evaluación de riesgos sea el motor que impulse un mayor trabajo sobre la elaboración y el uso de modelos.

Palabras clave
Emergencia sanitaria – Epidemiología – Modelo combinado – Modelo sencillo – Red – Riesgo.

References

1. Anderson R.M. & May R.M. (1979). – Population biology of infectious diseases: Part I. *Nature*, **280** (5721), 361-367.

2. Arkoosh M.R., Casillas E., Clemons E., Kagley A.N., Olson R., Reno P. & Stein J.E. (1998). – Effect of pollution on fish diseases: potential impacts on salmonid populations. *J. aquat. Anim. Hlth*, **10** (2), 182-190.

3. Arnio J., Brauer F., van den Driessche P., Watmough J. & Wu J. (2006). – Simple models for containment of a pandemic. *J. roy. Soc. Interface*, **3** (8), 453-457.

4. Asplin L., Boxaspen K. & Sandvik A.D. (2004). – Modelling distribution of salmon lice in a Norwegian fjord. *In* Proc. Annual Science Conference of the International Council for the Exploration of the Sea (ICES CM 2004/P:11), Vigo, Spain. ICES, Copenhagen, 12 pp.

5. Asplin L., Salvanes A.G.V. & Kristoffersen J.B. (1999). – Nonlocal wind driven fjord-coast advection and its potential effect on plankton and fish recruitment. *Fish. Oceanog.*, **8** (4), 255-263.

6. Borsuk M.E., Reichert P., Peter A., Schager E. & Burkhardt-Holm P. (2006). – Assessing the decline of brown trout (*Salmo trutta*) in Swiss rivers using a Bayesian probability network. *Ecol. Modell.*, **192** (1-2), 224-244.

7. Bosetti V. & Pearce D. (2003). – A study of environmental conflict: the economic value of Grey Seals in southwest England. *Biodivers. Conserv.*, **12** (12), 2361-2392.

8. Brooks K.M. (2005). – The effects of water temperature, salinity, and currents on the survival and distribution of the infectious copepodid stages of sea lice (*Lepeophtheirus salmonis*) originating on Atlantic salmon farms in the Broughton Archipelago of British Columbia, Canada. *Rev. Fish. Sci.*, **13** (3), 177-204.

9. Brun E., Poppe T., Skrudland A. & Jarp J. (2003). – Cardyomyopathy syndrome in farmed Atlantic salmon *Salmo salar*. Occurrence and direct financial losses for Norwegian aquaculture. *Dis. aquat. Organisms.*, **56** (3), 241-247.

10. Bull J.J. (1994). – Perspective: virulence. *Evolution*, **48** (5), 1423-1437.

11. Chattopadhyay J. & Bairagi N. (2001). – Pelicans at risk in Salton Sea: an eco-epidemiological model. *Ecol. Modell.*, **136** (2-3), 103-112.

12. Corsin F., Turnbull J.F., Hao N.V., Mohan C.V., Phi T.T., Phuoc L.H., Tinh N.T.N. & Morgan K.L. (2001). – Risk factors associated with white spot syndrome virus infection in a Vietnamese rice-shrimp farming system. *Dis. aquat. Organisms*, **47** (1), 1-12.

13. Dann P., Norman F.I., Cullen J.M., Neira F.J. & Chiaradia A. (2000). – Mortality and breeding failure of little penguins, *Eudyptula minor*, in Victoria, 1995-1996, following a widespread mortality of pilchard, *Sardinops sagax*. *Mar. Freshwater Res.*, **51** (4), 355-362.

14. Denholm I. & Rowland M.W. (1992). – Tactics for managing pesticide resistance in arthropods: theory and practice. *Annu. Rev. Entomol.*, **37**, 91-112.

15. Des Clers S. (1993). – Modelling the impact of disease induced mortality on the population size of wild salmonids. *Fish. Res.*, **17** (1-2), 237-248.

16. Des Clers S. & Anderson K. (1995). – Sealworm (*Pseudoterranova decipiens*) transmission to fish trawled from Hvaler, Oslofjord, Norway. *J. Fish Biol.*, **46** (1), 8-17.

17. Des Clers S.A. & Wootten R. (1990). – Modelling population dynamics of the sealworm *Pseudoterranova decipiens*. *Neth. J. Sea Res.*, **25** (1-2), 291-299.

18. Dobson A.P. & May R.M. (1987). – The effects of parasites on fish populations – theoretical aspects. *Int. J. Parasitol.*, **17** (2), 363-370.

19. Fenton A., Hakalahti T., Bandilla M. & Valtonen E.T. (2006). – The impact of variable hatching rates on parasite control: a model of an aquatic ectoparasite in a Finnish fish farm. *J. appl. Ecol.*, **43** (4), 660-668.

20. Fletcher W.J. (1992). – Use of a spatial model to provide initial estimates of stock size for a purse seine fishery on pilchards (*Sardinops sagax neopilchardus*) in Western Australia. *Fish. Res.*, **14** (1), 41-57.

21. Ford S., Powell E., Klinck J. & Hofmann E. (1999). – Modeling the MSX parasite in eastern oyster (*Crassostrea virginica*) populations. I. Model development, implementation, and verification. *J. Shellfish Res.*, **18** (2), 475-500.

22. Frank S.A. (1996). – Models of parasite virulence. *Q. Rev. Biol.*, **71** (1), 37-78.

23. Fraser C., Riley S., Anderson R.M. & Ferguson N.M. (2004). – Factors that make infectious disease outbreak controllable. *Proc. natl Acad. Sci. USA*, **101** (16), 6146-6151.

24. Gillibrand P.A. & Willis K. (2007). – Dispersal of sea louse larvae from salmon farms: modelling the influence of environmental conditions and larval behaviour. *Aquat. Biol.*, **1** (1), 63-75.

25. Gustafson L.L., Ellis S.K., Beattie M.J., Chang B.D., Dickey D.A., Robinson T.L., Marenghi F.P., Moffett P.J. & Page F.H. (2007). – Hydrographics and the timing of infectious salmon anemia outbreaks among Atlantic salmon (*Salmo salar* L.) farms in the Quoddy region of Maine, USA and New Brunswick, Canada. *Prev. vet. Med.*, **78** (1), 35-56.

26. Härkönen T., Dietz R., Reijnders P., Teilmann J., Harding K., Hall A., Brasseur S., Siebert U., Goodman S.J., Jepson P.D., Rasmussen T.D. & Thompson P. (2006). – The 1988 and 2002 phocine distemper virus epidemics in European harbour seals. *Dis. aquat. Organisms*, **68** (2), 115-130.

27. Hastings T., Olivier G., Cusack R., Bricknell I., Nylund A., Binde M., Munro P. & Allan C. (1999). – Infectious salmon anaemia. *Bull. Eur. Assoc. Fish Pathol.*, **19** (6), 286-288.

28. Heinecke R.D., Martinussen T. & Buchman K. (2007). – Microhabitat selection of *Gyrodactylus salaris* Malmberg on different salmonids. *J. Fish Dis.*, **30** (12), 733-743.

29. Hemmingsen W. & MacKenzie K. (2001). – The parasite fauna of the Atlantic cod, *Gadus morhua* L. *Adv. mar. Biol.*, **40**, 1-80.

30. Hess G.R., Randolph S.E., Arneberg P., Chemini C., Furlanello C., Harwood J., Roberts M.G. & Swinton J. (2002). – Spatial aspects of disease dynamics. *In* The ecology of wildlife diseases (P.J. Hudson, A. Rizzoli, B.T. Grenfell, H. Heesterbeek & A.P. Dobson, eds). Oxford University Press, 102-118.

31. Heuch P.A. & Mo T.A. (2001). – A model of salmon louse production in Norway: effects of increasing salmon production and public management measures. *Dis. aquat. Organisms*, **45** (2), 145-152.

32. Hill B. (2002). – National and international impacts of white spot disease of shrimp. *Bull. Eur. Assoc. Fish Pathol.*, **22** (2), 58-65.

33. Hofmann E.E., Powell E.N., Klinck J.M. & Saunders G. (1995). – Modelling diseased oyster populations. I. Modelling *Perkinsus marinus* infection in oysters. *J. Shellfish Res.*, **14** (1), 121-151.

34. Jarp J., Gjevre A.G., Olsen A.B. & Bruheim T. (1994). – Risk factors for furunculosis, infectious pancreatic necrosis and mortality in post-smolt Atlantic salmon *Salmo salar* L. *J. Fish Dis.*, **18** (1), 67-78.

35. Jarp J. & Karlsen E. (1997). – Infectious salmon anaemia (ISA) risk factors in sea-cultured Atlantic salmon *Salmo salar*. *Dis. aquat. Organisms*, **28** (2), 79-86.

36. Jarp J., Tangen K., Willumsen F.V., Djupvik H.O. & Tveit A.M. (1993). – Risk factors for infection with *Aeoromas salmonicida* subsp. *salmonicida* in Norwegian freshwater hatcheries. *Dis. aquat. Organisms*, **17**, 81-86.

37. Jones M.W., Sommerville C. & Wootten R. (1992). – Reduced sensitivity of the salmon louse, *Lepeophtheirus salmonis*, to the organophosphate dichlorvos. *J. Fish Dis.*, **15** (2), 197-202.

38. Jorgensen S.E. (1988). – Fundamentals of ecological modelling. Developments in Environmental Modelling 9. Elsevier, Amsterdam, 391 pp.

39. Kao R.R. (2002). – The role of mathematical modelling in the control of the 2001 FMD epidemic in the UK. *Trends Microbiol.*, **10** (6), 279-286.

40. Kitching R.P., Thrusfield M.V. & Taylor N.M. (2006). – Use and abuse of mathematical models: an illustration from the 2001 foot and mouth disease epidemic in the United Kingdom. *In* Biological disasters of animal origin: the role and preparedness of veterinary and public health services (M. Hugh-Jones, ed.). *Rev. sci. tech. Off. int. Epiz.*, **25** (1), 293-311.

41. Klinck J.M., Powell E.N., Kraeuter J.N., Ford S.E. & Ashton-Alcox K.A. (2001). – A fisheries model for managing the oyster fishery during times of disease. *J. Shellfish Res.,* **20** (3), 977-989.

42. Krkosek M., Lewis M.A., Morton A., Frazer L.N. & Volpe J.P. (2006). – Epizootics of wild fish induced by farm fish. *Proc. natl Acad. Sci. USA*, **103** (42), 15506-15510.

43. Krkosek M., Lewis M.A. & Volpe J.P. (2005). – Sea lice interactions between salmon farms and out-migrant juvenile salmon. *Proc. roy. Soc. Lond., B, biol. Sci.*, **272** (1564), 689-696.

44. Kuris A.M. & Lafferty K.D. (1991). – Modelling crustacean fisheries: effects of parasites on management strategies. *Can. J. Fish. aquat. Sci.*, **49**, 327-336.

45. Lafferty K.D., Porter J.W. & Ford S.E. (2004). – Are diseases increasing in the ocean? *Annu. Rev. Ecol. Evol. Syst.*, **35**, 31-54.

46. Lawrence K.S. (2005). – Assessing the value of recreational sea angling in South West England. *Fish. Manag. Ecol.*, **12** (6), 369.

47. Lenormand T. & Raymond M. (1998). – Resistance management: the stable zone strategy. *Proc. roy. Soc. Lond., B, biol. Sci.*, **265** (1409), 1985-1990.

48. Leung P. & Tran L.T. (2000). – Predicting shrimp disease occurrence: artificial neural networks vs. logistic regression. *Aquaculture*, **187** (1-2), 35-49.

49. Liao C.-M., Chang C.-F., Yeh C.-H., Chen S.-C., Chiang K.-C., Chio C.-P., Chou B.Y.-H., Jou L.-J., Lien G.-W., Lin C.-M., Shen H.-H. & Wu G.-D. (2006). – Metal stresses affect the population dynamics of disease transmission in aquatic species. *Aquaculture*, **257** (1-4), 321-332.

50. Lillehaug A. (1989). – A cost-effectiveness study of three different methods of vaccination against vibriosis in salmonids. *Aquaculture*, **83** (3-4), 227-236.

51. Lipsitch M., Bergstrom C.T. & Levin B.R. (2000). – The epidemiology of antibiotic resistance in hospitals: paradoxes and prescriptions. *Proc. natl Acad. Sci. USA*, **97** (4), 1938-1943.

52. Lorenzen K., des Clers S.A. & Anders K. (1991). – Population dynamics of lymphocytosis disease in estuarine flounder, *Platichthys flesus* (L.). *J. Fish Biol.*, **39**, 577-587.

53. Lotz J.M., Flowers A.M. & Breland V. (2003). – A model of Taura syndrome virus (TSV) epidemics in *Litopenaeus vannamei*. *J. Invertebr. Pathol.*, **83** (2), 168-176.

54. Lotz J.M. & Soto M.A. (2002). – Model of white spot syndrome virus (WSSV) epidemics in *Litopenaeus vannamei*. *Dis. aquat. Organisms*, **50** (3), 199-209.

55. McCallum H., Barlow N. & Hone J. (2001). – How should pathogen transmission be modelled? *Trends Ecol. Evol.*, **16** (6), 295-300.

56. McCallum H.I., Kuris A., Harvell C.D., Lafferty K.D., Smith G.W. & Porter J. (2004). – Does terrestrial epidemiology apply to marine systems? *Trends Ecol. Evol.*, **19** (11), 585-591.

57. McCausland W.D., Mente E., Pierce G.J. & Theodossiou I. (2006). – A simulation model of sustainability of coastal communities: aquaculture, fishing, environment and labour markets. *Ecol. Modell.*, **193** (3-4), 271-294.

58. Martin P.A.J., Cameron A.R. & Greiner M. (2007). – Demonstrating freedom from disease using multiple data sources 1: a new methodology based on scenario trees. *Prev. vet. Med.*, **79** (2) 71-97.

59. Marty G.D., Quinn T.J., Carpenter G., Meyers T.R. & Willits N.H. (2003). – Role of disease in abundance of a Pacific herring (*Clupea pallasi*) population. *Can. J. Fish. aquat. Sci.*, **60** (10), 1258-1265.

60. May R.M. & Anderson R.M. (1979). – Population biology of infectious diseases: Part II. *Nature*, **280** (5722), 455-461.

61. Moran D. & Fofana A. (2007). – An economic evaluation of the control of three notifiable fish diseases in the United Kingdom. *Prev. vet. Med.*, **80** (2-3), 193-208.

62. Murray A.G. (2004). – Managing harvesting to minimize the impact of epidemics on wild fish stocks. *Natl Res. Model.*, **17** (2), 103-121.

63. Murray A.G. (2006). – A model of the emergence of infectious pancreatic necrosis virus in Scottish salmon farms 1996-2003. *Ecol. Modell.*, **199** (1), 64-72.

64. Murray A.G., Amundrud T.L. & Gillibrand P.A. (2005). – Models of hydrodynamic pathogen dispersal affecting Scottish salmon production: modelling shows how Scotland eradicated ISA, but not IPN. *Bull. Aquacult. Assoc. Canada*, **105** (1), 79-86.

65. Murray A.G. & Gaughan D.J. (2003). – Using an age-structured model to simulate the recovery of the Australian pilchard (*Sardinops sagax*) population following epidemic mass mortality. *Fish. Res.*, **60** (2-3), 415-426.

66. Murray A.G. & Gillibrand P.A. (2006). – Modelling dispersal of salmon lice in Loch Torridon, Scotland. *Mar. Pollut. Bull.*, **53** (1-4), 128-135.

67. Murray A.G. & Jackson G.A. (1993). – Viral dynamics II. A model of the effects of ultraviolet light and mixed-layer circulation on virus survival in seawater. *Mar. Ecol. Progr. Series*, **102**, 105-114.

68. Murray A.G. & O'Callaghan M. (2005). – The numerical and programming methods used to implement models of the spread and impact of a major epidemic disease: pilchard herpesvirus, Australia 1995 and 1998/9. *Environ. Modell. Software*, **20** (5), 575-585.

69. Murray A.G., O'Callaghan M. & Jones B. (2001). – Simple models of massive epidemics of herpesvirus in Australian (and New Zealand) pilchards. *Environ. int.*, **27** (2-3), 243-248.

70. Murray A.G., O'Callaghan M. & Jones B. (2003). – A model of spatially-evolving herpesvirus epidemics causing mass mortality in Australian pilchards (*Sardinops sagax*). *Dis. aquat. Organisms*, **54** (1), 1-14.

71. Murray A.G. & Peeler E.J. (2005). – A framework for understanding the potential for emerging diseases in aquaculture. *Prev. vet. Med.*, **67** (2-3), 223-235.

72. Murray A.G., Smith R.J. & Stagg R.M. (2002). – Shipping and the spread of infectious salmon anemia in Scottish aquaculture. *Emerg. infect. Dis.*, **8** (1), 1-5.

73. Nérette P., Dohoo I. & Hammel L. (2005). – Estimation of specificity and sensitivity of three diagnostic tests for infectious salmon anaemia virus in the absence of a gold standard. *J. Fish Dis.*, **26** (2), 89-99.

74. Ogut H. & Bishop S.C. (2007). – A stochastic modelling approach to describing the dynamics of an experimental furunculosis epidemic in Chinook salmon, *Oncorhynchus tshawytscha* (Walbaum). *J. Fish Dis.*, **30** (2), 93-100.

75. Ogut H., LaPatra S.E. & Reno P.W. (2005). – Effects of host density on furunculosis epidemics determined by the simple SIR model. *Prev. vet. Med.*, **71** (1-2), 83-90.

76. Ogut H., Reno P.W. & Sampson D. (2004). – A deterministic model for the dynamics of furunculosis in Chinook salmon *Oncorhynchus tshawytscha*. *Dis. aquat. Organisms*, **62** (1-2), 57-63.

77. Paisley L.G., Karlsen E., Jarp J. & Mo T.A. (1999). – A Monte Carlo simulation model for assessing the risk of introduction of *Gyrodactylus salaris* to the Tana river, Norway. *Dis. aquat. Organisms*, **37** (2), 145-152.

78. Pal S., Kunda K. & Chattopadhyay J. (2006). – Role of standard incidence in an eco-epidemiological system: a mathematical study. *Ecol. Modell.*, **199** (3), 229-239.

79. Patterson K.R. (1996). – Modelling the impact of disease-induced mortality in an exploited population of the fungal parasite *Ichthyophonus hoferi* in the North Sea herring (*Clupea harengus*). *Can. J. Fish. aquat. Sci.*, **53** (12), 2870-2877.

80. Pauly D., Christensen V. & Walters C. (2000). – Ecopath, ecosim, and ecospace as tools for evaluating ecosystem impact of fisheries *ICES. J. mar. Sci.*, **57** (3), 697-706.

81. Peddie S. & Stott A. (2003). – Applying animal health economics to fish health management. *Fish vet. J.*, **7**, 1-17.

82. Peeler E.J., Murray A.G., Thebault A., Brun E., Giovaninni A. & Thrush M.A. (2007). – The application of risk analysis in acuatic health management. *Prev. vet. Med.*, **81** (1-3), 3-20.

83. Pike A.W. & Wadsworth S.L. (1999). – Sealice on salmonids: their biology and control. *Adv. Parasitol.*, **44**, 231-337.

84. Poillot R., Gerbier G. & Gardner I.A. (2002). – 'TAGS' a program for evaluation of test accuracy in the absence of a gold standard. *Prev. vet. Med.*, **53** (1-2), 67-81.

85. Reno P.W. (1998). – Factors involved in the dissemination of disease in fish populations. *J. aquat. Anim. Hlth*, **10** (2), 160-171.

86. Revie C.W., Hollinger E., Gettinby G., Lees F. & Heuch P.A. (2007). – Clustering of parasites within cages on Scottish and Norwegian salmon farms: alternative sampling strategies illustrated using simulation. *Prev. vet. Med.*, **81** (1-3), 135-147.

87. Revie C.W., Robbins C., Gettinby G., Kelly L. & Treasurer J.W. (2005). – A mathematical model of the growth of sea lice, *Lepeophtheirus salmonis*, populations on farmed Atlantic salmon, *Salmo salar* L., in Scotland and its use in assessment of treatment strategies. *J. Fish Dis.*, **28** (10), 603-613.

88. Rodgers C.J. (ed.) (2001). – Risk analysis in aquatic animal health. Proc. of an International Conference held in Paris, 8-10 February 2000. World Organisation for Animal Health, Paris, 346 pp.

89. Rohani P., Green C.J., Mantilla-Beniers N.B. & Grenfell B.T. (2003). – Ecological interference between fatal diseases. *Nature*, **422** (6934), 885-888.

90. Ruane N.M., Murray A.G., Geoghegan F., Raynard R.S. (in prep). – Modelling the initiation and spread of infectious pancreatic necrosis virus in the Irish salmon industry: the role of imports. In preparation.

91. Scheel I., Aldrin M., Frigessi A. & Jansen P.A. (2007). – A stochastic model for infectious salmon anemia (ISA) in Atlantic salmon farming. *J. roy. Soc. Interface*, **4** (15) (DOI: 10.1098/rsif.2007.0217).

92. Sharkey K.J., Fernandez C., Morgan K.L., Peeler E., Thrush M., Turnbull J.F. & Bowers R.G. (2006). – Pair-level approximations to the spatio-temporal dynamics of epidemics on asymmetric contact networks. *J. math. Biol.*, **53** (1), 61-85.

93. Skall H.F., Olesen N.J. & Mellergaard S. (2005). – Prevalence of viral haemorrhagic septicaemia virus in Danish marine fishes and its occurrence in new host species. *Dis. aquat. Organisms*, **66** (2), 145-151.

94. Smith G., Bebak J. & McAllister P.E. (2000). – Experimental infectious pancreatic necrosis infections: propagative or point-source epidemic? *Prev. vet. Med.*, **47** (4), 221-241.

95. Snieszko S.F. (1973). – Recent advances in scientific knowledge and developments pertaining to diseases of fishes. *Adv. vet. Sci. comp. Med.*, **17**, 291-314.

96. Stärk K.D.C., Regula G., Hernandez J., Knopf L., Fuchs K., Morris R.S. & Davies P. (2006). – Concepts for risk-based surveillance in the field of veterinary medicine and veterinary public health: review of current approaches. *BMC Hlth Serv. Res.*, **6**, 1-8.

97. Stein A., Bjorn P.A., Heuch P.A. & Elston D.A. (2005). – Population dynamics of salmon lice *Lepeophtheirus salmonis* on Atlantic salmon and sea trout. *Mar. Ecol. Progr. Series*, **290**, 263-275.

98. Strucchi D.J., Henry R.F. & Foreman M.G.G. (2005). – Modelling the transport and dispersion of IHN pathogens in Broughton Archipelago, British Columbia. *Bull. Aquacult. Assoc. Canada*, **105** (1), 52-59.

99. Swinton J., Harwood J., Grenfell B.T. & Gilligan C.A. (1998). – Persistence thresholds for phocine distemper virus in harbour seals *Phoca vitulina* metapopulations. *J. anim. Ecol.*, **67** (1), 54-68.

100. Thebault A., Peeler E.J., Murray A.G., Brun E., Giovaninni A. & Thrush M.A. (2007). – Application de la modélisation en santé des espèces aquacoles. *INRA Prod. anim.*, **20** (3), 223-226.

101. Thrush M. & Peeler E. (2006). – Stochastic simulation of live fish movements in England and Wales to predict potential spread of exotic pathogens. *Dis. aquat. Organisms*, **72** (2), 115-123.

102. Treasurer J.W. (2002). – A review of potential pathogens of sea lice and the application of cleaner fish in biological control. *Pest Manag. Sci.*, **58** (6), 546-558.

103. Treasurer J.W., Wadsworth S. & Grant A. (2000). – Resistance of sea lice, *Lepeophtheirus salmonis* (Krøyer), to hydrogen peroxide on farmed Atlantic salmon, *Salmo salar* L. *Aquacult. Res.*, **31** (11), 855-860.

104. Tucker C.S., Norman R., Shinn A.P., Bron J.E., Sommerville C. & Wootten R. (2002). – A single cohort time delay model of the life-cycle of the salmon louse *Lepeophtheirus salmonis* on Atlantic salmon *Salmo salar*. *Fish Pathol.*, **37** (3), 107-118.

105. Vincent A.G. & Lotz J.M. (2007). – Advances in research of necrotizing hepatopancreatitis bacterium (NHPB) affecting penaeid shrimp aquaculture. *Rev. Fish. Sci.*, **15** (1/2), 63-73.

106. Vose D. (2000). – Risk analysis: a quantitative guide. John Wiley and Sons, Chichester, England, 418 pp.

107. Ward T.M., Hoedt F., McLeay L., Dimmlich W.F., Jackson G., Rogers P.J. & Jones B. (2001). – Have recent mass mortalities of the sardine *Sardinops sagax* facilitated an expansion in the distribution and abundance of the anchovy *Engraulis australis* in South Australia? *Mar. Ecol. Progr. Series*, **220**, 241-251.

108. Watts D.J. & Strogatz S.H. (1998). – Collective dynamics of 'small-world' networks. *Nature*, **393** (6684), 440-442.

109. White P.C.L., Jennings N.V., Renwick A.R. & Barker N.H.L. (2005). – Questionnaires in ecology: a review of past use and recommendations for best practice. *J. appl. Ecol.*, **42** (3), 421-430.

110. Whittington R., Crockford M. & Jones B. (2006). – Survey design for herpesvirus in pilchard, a marine pelagic finfish. *In* Proc. of the 11th Symposium of the International Society for Veterinary Epidemiology and Economics, 6-11 August, Cairns, Australia: ISVEE XI.

111. Wilson K., Bjørnstad O.N., Dobson A.P., Merler S., Poglayen G., Randolph S.E., Read A.F. & Skorping A. (2002). – Heterogeneities in macroparasite infections: patterns and processes. *In* The ecology of wildlife diseases (P.J. Hudson, A. Rizzoli, B.T. Grenfell, H. Heesterbeek & A.P. Dobson, eds), Oxford Biology, Oxford, 6-44.

112. Wooldridge S., Done T., Berkelmans R., Jones R. & Marshall P. (2005). – Precursors for resilience in coral communities in a warming climate: a belief network approach. *Mar. Ecol. Progr. Series*, **295**, 157-169.

113. Yokota M. & Watanabe S. (2004). – Risk analysis of epidemic disease on one-dimensional cultured fish pond model. *Nippon Suisan Gakkaishi*, **70** (6), 889-895.