



## International Polar Year 2007-2008 The Netherlands (IPY•NL)



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### **Combining behaviour-based and epidemiological models to identify the role of Arctic breeding migratory waterfowl in the ecology of infectious diseases, notably Avian Influenza**

#### Abstract

In contrast to expectations of the last century that infections could be brought under control, today we increasingly face threats from new emerging agents, transcending species boundaries, entering new geographic areas but also from well-known agents that turn out to be very persistent, escape immunity, that are difficult to control in outbreaks or that continuously evolve and thus, escape existing treatments.

Avian influenza excellently exemplifies these issues: it has repeatedly crossed species-boundaries (e.g. from wild waterfowl to poultry species), continues to escape immunity by frequent mutations and is thus difficult to control in outbreaks. Although it will be impossible to prevent such outbreaks, a fundamental understanding of the origin and spread of influenza viruses (IV) through animal and human populations may play a key role in designing strategies to recognize the threats early and to minimize the risk of outbreaks.

Therefore, we aim to combine epidemiological and behaviour-based models and in particular, to shed light on the role of migratory waterfowl in the spread of infectious diseases by successively testing the assumptions of 1) Within-individual processes: Testing consequences of IV infections on individuals, e.g. on reproductive success, mortality; 2) Between-individual processes: What are the population-level consequences and patterns given the assumptions under 1) and transmission rates/ modes (local and individual events)? For both, we will identify the conditions under which IV may persist in a host-population and determine characteristics of the spatio-temporal spread of IV among populations. Thus, combining epidemiology and bird migration in such model will identify key times and places for the spread of infectious diseases as well as sensitive parts in the dynamics of hosts and pathogens and thereby, provide a basis for potential management actions.



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**Is this application part of a *coordinating project proposal*?** X Yes

If the above question is answered with "yes", please fill in the title of the coordinating project proposal.

Title coordinating project proposal: Bird health

**Related international IPY 'Full proposal'**

(submitted to ICSU-WMO Joint Committee for IPY)

Title: Bird Health

Lead contact (name, organisation, country): Dr. Maarten J.J.E. Loonen, Arctic Centre,  
University of Groningen, The Netherlands

ID No: 172

Website URL for more information: [www.birdhealth.nl](http://www.birdhealth.nl)

**Geographic area of interest for this (IPY•NL) application**

X Arctic

**1a. Further details of the applicant(s)**

**Main applicant**

Gender: Male  
Tenure Position: Yes  
Research School: Animal Health/Life Sciences (i.o)  
Website URL:

**Co-applicant**

Gender: Male  
Tenure Position: Yes  
Research School: Functional Ecology  
Website URL: <http://www.nioo.knaw.nl/ppages/mklaassen/>

**1b. Alternative contact**

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**1c. Does the local authority support your application?** Yes

(did you inform your superior and accepts your institute/university the conditions for support by NWO)

**1d. Renewed application?** No

(in case of renewed application please summarize main changes under item 4) **Dossier nr:**

**1e. Applying for:** PostDoc

(for PhD student please underline promotor in question 1f, composition of research group)



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## 1f. Composition of the research group

Name and title	Specialization	Employment/Institute
Prof. Dr. J.A.P. Heesterbeek Dr. A. Bouma	Modelling infectious diseases	Theoretical Epidemiology, Faculty of Veterinary Medicine Utrecht University (FVU)
Prof. Dr. M. Klaassen Dr. S. Bauer Dr. J. van Gils Dr. B.A. Nolet	Bird migration, population dynamics Modelling bird migration Spatial dynamics in birds Waterfowl ecology	NIOO-KNAW
Dr. R. Fouchier Drs. V.J. Munster	Virology Influenza virus surveillance	Dept. Virology Erasmus Medical Centre (EMC)
Dr. M.J.J.E.Loonen	Arctic ecology, geese	Arctic Centre, University of Groningen

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## 2. Populaire samenvatting van de aanvraag (Nederlands)

(if granted, this description will be used for Dutch communication, also to non-specialists)

Trekvogels kunnen vogelgriep verspreiden. In dit verband bestaat er grote onrust over de mogelijke consequenties voor de volksgezondheid, daar vogelgriep ook op mensen en andere dieren kan overspringen en vervolgens in zeer gevaarlijke varianten kan muteren. Uit onderzoek is gebleken dat Arctische watervogels een belangrijke bron en verspreidingsvector voor vogelgriep kunnen zijn. Het is echter niet bekend hoe precies de natuurlijke cyclus van de vogelgriepvirussen en de natuurlijke cyclus van migrerende watervogels met elkaar verbonden zijn en elkaar beïnvloeden. In dit project onderzoeken we de dynamica van deze twee cycli. Op epidemiologische, ecologische en gedragsinzichten gebaseerde wiskundige modellen worden hiervoor als hulpmiddel gebruikt. We zijn dan in staat om, samen met de biologische kennis die wordt opgedaan in een zusterproject, inzicht te krijgen in de vraag hoe de jaarlijkse trekvogelcyclus als motor kan fungeren voor de overleving, vernieuwing en verspreiding van het griepvirus.

## 3a. Top 5 scientific publications of the applicants related to the proposed research

1. Diekmann, O. and **J.A.P. Heesterbeek**. 2000. *Mathematical Epidemiology of Infectious Diseases: model building, analysis and interpretation*. John Wiley and Sons, Chichester.
  2. **Klaassen, M., Bauer, S., Madsen, J. & Tombre, I.** 2005. Modelling behavioural and fitness consequences of disturbance for geese along their spring flyway. *Journal of Applied Ecology* ("in press")
  3. Roberts, M.G. and **J.A.P. Heesterbeek** 2003: A new method to estimate the effort required to control an infectious disease. *Proceedings of the Royal Society London, Series B*, 270, 1359-1364.
  4. Etienne, R.S. and **J. A. P. Heesterbeek**. Rules of thumb for conservation of metapopulations based on a stochastic winking-patch model. *American Naturalist* 158 (4):389-407, 2001.
  5. **Nolet, B.A., Bevan, R.M., Klaassen, M., Langevoord, O. & Van der Heijden, Y.G.J.T.** 2002. Habitat switching by Bewick's swans: maximisation of average long-term energy gain? *J Anim Ecol* 71: 979-993.
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### 3b. Other relevant publications (max 1 page for publications, min 10 pts)

By the applying research group:

#### FVM

- Neutel, A.M., **J.A.P. Heesterbeek** and P.C. de Ruiter. 2002. Weak links in the long loops enhance stability in real food webs. *Science*, 296, 1120-1123.
- Stegeman, A., **Bouma**, A. Elbers A.R., de Jong, M.C. Nodelijk, G., de Klerk, F. Koch, G., van Boven, M. 2003. Avian Influenza A virus (H7N7) epidemic in the Netherlands in 2003: course of the epidemic and effectiveness of control measures. *Journal of Infectious Diseases*, 190(12): 2088-2095.
- Hudson, P.J., Rizzolli, A., Grenfell, B.T., **J.A.P. Heesterbeek**, and Dobson, A.P. 2002: The ecology of wildlife diseases. Oxford University Press, Oxford.
- De Jong, M.C.M., **A. Bouma**, O. Diekmann, and **H. Heesterbeek**. Modelling transmission: mass action and beyond. *Trends in Ecology & Evolution* 17 (2):64, 2002.

#### NIOO

- Beekman, J.H., **Nolet, B.A. & Klaassen, M.** 2002. Skipping swans: differential use of migratory stopover sites in spring and autumn in relation to fuelling rates. *Ardea* 90(3):437-460.
- Clausen, P., **Nolet, B.A.**, Fox, A.D. & **Klaassen, M.** 2002. Long-distance endozoochorous dispersal of submerged macrophyte seeds by migratory waterbirds in northern Europe - a critical review of possibilities and limitations. *Acta Oecologica* 23: 191-203.
- Klaassen, M & Santamaría, L.** (eds.) 2002. Dispersal of Aquatic Organisms, The role of waterbirds. Special issue *Acta Oecologia* Vol 23(3).
- Klaassen, M.**, Lindström, Å., Meltofte, H. & Piersma, T. 2001. Arctic waders are no capital breeders. *Nature* 413: 794.
- Madsen, J., **Klaassen, M.** 2005. Assessing body condition and energy budget components by scoring abdominal profiles in free-ranging geese. *J Avian Biol* ("in press")
- Nolet, B.A.**, Klaassen, R.H.G. & Mooij, W.M. 2006. The use of a flexible patch leaving rule under exploitative competition: a field test with swans. *Oikos* (in press)

#### EMC

- Fouchier, R.A.M.**, Bestebroer, T.M., Herfst, S., van der Kemp, L., Rimmelzwaan, G.F. & Osterhaus, A.D.M.E. 2000. Detection of influenza A viruses from different species by PCR amplification of conserved sequences in the matrix gene. *Journal of Clinical Microbiology* 38:4096-4101.
- Fouchier, R.A.M.**, Olsen, B, Bestebroer, T.M., Herfst, S., van der Kemp, L., Rimmelzwaan, G.F. & Osterhaus A.D.M.E. 2003a. Influenza A virus surveillance in wild birds in Northern Europe in 1999 and 2000. *Avian Diseases* 47: 857-860.
- Kuiken, T., **Fouchier, R.A.M.**, Rimmelzwaan, G.F., & Osterhaus, A.D.M.E. 2003b. Emerging viral infections in a rapidly changing world. *Current Opinion in Biotechnology* 14:641-646.
- Fouchier, R.A.M.**, Schneeberger, P.M., Rozendaal, F.W., Broekman, J.M., Kemink, S.A.G., **Munster, V.**, Kuiken T., Rimmelzwaan, G.F., Schutten, M., van Doornum, G.J.J., Koch, G., Bosman, A., Koopmans, M & Osterhaus, A.D.M.E. 2004. Avian influenza A (H7N7) virus associated with human conjunctivitis and a fatal case of acute respiratory distress syndrome. *Proceedings of the National Academy of Sciences, USA* 101:1356-1361.
- Fouchier, R.A.M.**, **Munster, V.**, Wallensten, A., Bestebroer, T.M., Herfst, S., Smith, D., Rimmelzwaan, G.F., Olsen, B., & Osterhaus, A.D.M.E. 2005a. Characterization of a novel influenza A virus hemagglutinin subtype (H16) obtained from black-headed gulls. *J Virol* 79:2814-2822.
- Fouchier, R.A.M.**, Kuiken, T., Rimmelzwaan, G.F., & Osterhaus, A.D.M.E. 2005b. The threat of avian influenza; the need to link human and animal health through a global influenza task force. *Nature*, In press.

#### Other references with respect to the application:

- Krauss, S., Walker, D., Pryor, S.P., Niles, L., Chenghong, L., Hinshaw, V.S., Webster, R.G. 2004. Influenza A viruses of migrating wild aquatic birds in North America. *Vector-Borne and Zoonotic Diseases* 4: 177-189.
- Houston, A.I. and J. M. McNamara. *Models of adaptive behaviour: An approach based on state*, Cambridge:Cambridge University Press, 1999.



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### 4. Detailed description of research area and research plan

(max 4 pages, min 10 pts, including figures)

(Objectives, innovative aspects, history/background, scientific approach and research methodology)

#### Introduction

Infectious diseases have an impact on animals and humans that continues to increase and diversify. In contrast to expectations of the last century that infections could be brought under control, today we increasingly face threats from new emerging agents, transcending species boundaries, entering new geographic areas but also from well-known agents that turn out to be very persistent, escape immunity, that are difficult to control in outbreaks or that continuously evolve and thus, escape existing treatments. One of the reasons why infectious diseases are so successful is that nowadays people and animals all over the world are in contact with each other. Furthermore, both people and farm animals live in high densities and closely together and thus enhance the possibility for zoonoses.

Avian influenza excellently exemplifies these issues: it has repeatedly crossed species-boundaries (e.g. from wild waterfowl to poultry species, from birds to mammals), and continues to escape immunity by frequent mutations and is thus difficult to control in outbreaks. Especially, the outbreaks of highly pathogenic avian influenza (HPAI or fowl plague) in the Netherlands (2003), and South-East Asia (1997-2005) has shown the threats of HPAI in animals and humans. Although it will be impossible to prevent such outbreaks, a fundamental understanding of the origin and spread of influenza viruses (IV) through animal and human populations may play a key role in designing strategies to recognize the threats early and to minimize the risk of outbreaks.

However, much in the ecology of (avian) influenza remains unclear. In the current expanding outbreak of H5N1, a strong role of migratory birds is conjectured in the Palaearctic. Notably ducks, geese and swans from Asian, European and the eastern Mediterranean regions breed in over-lapping areas in the Russian Arctic, and could in this way act as mixing and redistribution vessels for existing and new subtypes. The (multiple) virus subtype could well survive the winter in the cold water and re-infect birds upon their return the next spring. The dynamics of this life cycle and the dynamics in the wintering and breeding grounds is, however, poorly studied and poorly understood. Important questions relate to the effect of the virus on migrating birds; even if it does not kill the host, the effects on its fitness, behaviour and energy balance through energy and resources spent on immune reactions and morbidity can be such that the chances of successfully completing the migration are compromised. This type of insight is crucial in understanding the life cycle of IV and in realistic risk-estimation of particular sub-types spreading into new regions and threatening domestic waterfowl, free-ranging poultry, commercial poultry and human (in that temporal order).

Arctic breeding migratory waterfowl, notably geese and swans, may play a key role as reservoirs for avian IV. The transmission of IV between birds is thought to occur primarily via a faecal-oral route. Although many bird species are known to be potential carriers of IV, waterfowl are considered the prime host and vector for IV among birds because of their highly social behaviour during the non-breeding season and their association with water—an ideal medium for the survival and distribution of excreted viruses (e.g. Krauss et al. 2004)

In support of this hypothesis, the yearly peak in avian influenza occurs in late summer and early winter, coinciding with the southward migration of waterfowl from their Arctic breeding areas to the wintering grounds in temperate latitudes in Western Europe. For these species, the Arctic seems to be an important area for the exchange of avian IV as resulting from the following facts: 1) Many species and large numbers of waterfowl meet there during breeding and moulting; 2) The latter activities require 'hard work' and may thus leave individuals in a condition, in which they are particularly susceptible to infections; 3) During moulting, birds become flightless and therefore, concentrate on lakes and ponds, where IV might easily be exchanged between individuals but also survive the winter constituting a reservoir for (re-)infections in subsequent year(s).

While the idea of the Arctic as a melting pot for IV is an appealing scenario, this remains to be demonstrated. Alternative or additional hypotheses might include a paramount role of The Netherlands with its high densities of humans (16 million/41500 km<sup>2</sup>), pigs (20 million) and poultry (95 million) and its many lakes and waterways, its location just south of the 0 °C January isotherm and its intensive agricultural production. Furthermore, the Netherlands forms the most waterfowl dense area in Europe (e.g. 1.5 million wintering geese) and both in autumn and spring, it is a major staging site for waterfowl species that travel between their high latitude breeding areas and wintering areas in western Africa (notably Niger and Senegal deltas). Thus, all ingredients for HPAI outbreaks in animals and potential emergence of pandemic influenza are present in The Netherlands. Although many other places on our globe can be identified as high-risk areas for a pandemic influenza outbreak, the Netherlands is in an ideal position to study the role of Arctic breeding waterfowl as vectors for avian IV dispersal.

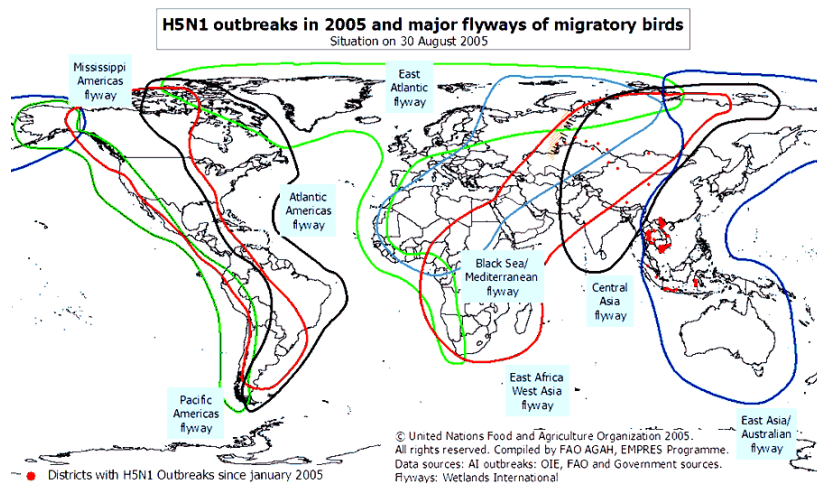


Fig.1. Flyways of migratory birds overlap in many regions. In the Russian Arctic, for instance, migratory waterfowl breed, moult and subsequently, return to their wintering grounds in Europe, the Middle East and Asia. This particular concurrence in the breeding grounds may facilitate the exchange of infectious diseases, which are then brought to the birds' respective wintering areas. (Source: United Nations Food and Agriculture Organisation)

However, we need a better understanding of within-host dynamics, between-host transmission as well as within and between-community spread of influenza in order to identify key areas and processes and eventually suggest efficient management actions. To this end, we plan to proceed in two steps – first, we aim to establish an empirical basis of the prevalence of IV in populations of migratory waterfowl and to identify its consequences on individual performance (which is outlined in detail in a sister application). Secondly, we will develop and link behaviour-based and epidemiological models to reveal which individual characteristics relate to susceptibility of individuals to IV infections, to link individual infection history to the population dynamics and consequently, to understand the spatio-temporal dynamics of IV within its host populations.

### Objectives

The general aim of this project is to investigate the link between the ecology of IV and long-distance migratory Arctic-breeding waterfowl, notably geese and swans. Therefore, we aim to combine epidemiological and behaviour-based models and in particular, we aim to shed light on the role of migratory waterfowl in the spread of IV and will successively test assumptions of 1) Within-individual processes: Testing consequences of IV infections on individuals, e.g. on movements, reproductive success, mortality; 2) Between-individual processes: What are the population-level consequences and patterns given the assumptions under 1) and transmission rates/modes (local and individual events)? For both, we will identify the conditions under which IV may persist in a host-population and determine characteristics of the spatio-temporal spread of IV among populations and thus, identify key times and places for IV dynamics. The latter may stimulate and guide empirical research (as described in companion application) and more importantly, establish the basis for potential management actions.

### Methodology

Model development, parameterisation and scrutiny require close collaboration of a multi-disciplinary team of virologists, waterfowl ecologists, epidemiologists and theoreticians. Mathematical models are an important tool to investigate population phenomena arising out of individual-level processes and interaction. An important biological basis for the model will be established in a sister-project, wherein a circumpolar screening of Arctic breeding geese and swans for IV will identify the spatio-temporal patterns of prevalence in a number of host species. Furthermore, the susceptibility to infections will be investigated as dependent on individual characteristics as well as the potential survival and reproductive consequences of infections.

#### 1. Behaviour-based models

A fundamental theme in ecology is to explain the number and distribution of animals. Behaviour-based models approach this question from an individual's perspective by considering behaviour as resulting from energetic constraints and from interactions with conspecifics and the environment.

Especially state-dependent optimisation models (Houston & McNamara 1999) have proved useful in understanding the behaviour of organisms as shaped by natural selection and have therefore the potential to integrate existing empirical knowledge, to identify gaps in our current knowledge, and thus, guide future empirical research.



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In such models, individuals are characterised by their state - a set of variables, which capture essential traits of the organism. In each time step, an individual may perform an action and the choice of a particular action is allowed to depend on the individual's state, and time of the year, and in turn, the action's costs and benefits will determine the individual's new state (see Fig. 2). In models of avian migration, the range of actions includes migratory, foraging and reproductive actions. The best action at any given time of the year depends on future behaviour, and hence on the best behaviour at all other times of the year. To find the strategy that maximises the number of descendants that an organism leaves far into the future we use dynamic programming; working backwards from the future.

Using the optimal strategy for all combinations of state variable values, we can simulate the behaviour of birds following this optimal routine and thus, generate spatially and temporally explicit predictions of the distribution of birds and specify the fitness consequences of animal movements. Additionally, such a model allows us also to follow the development of state variable values over time, e.g. body reserve dynamics, and to identify factors and processes crucially affecting migration schedules.

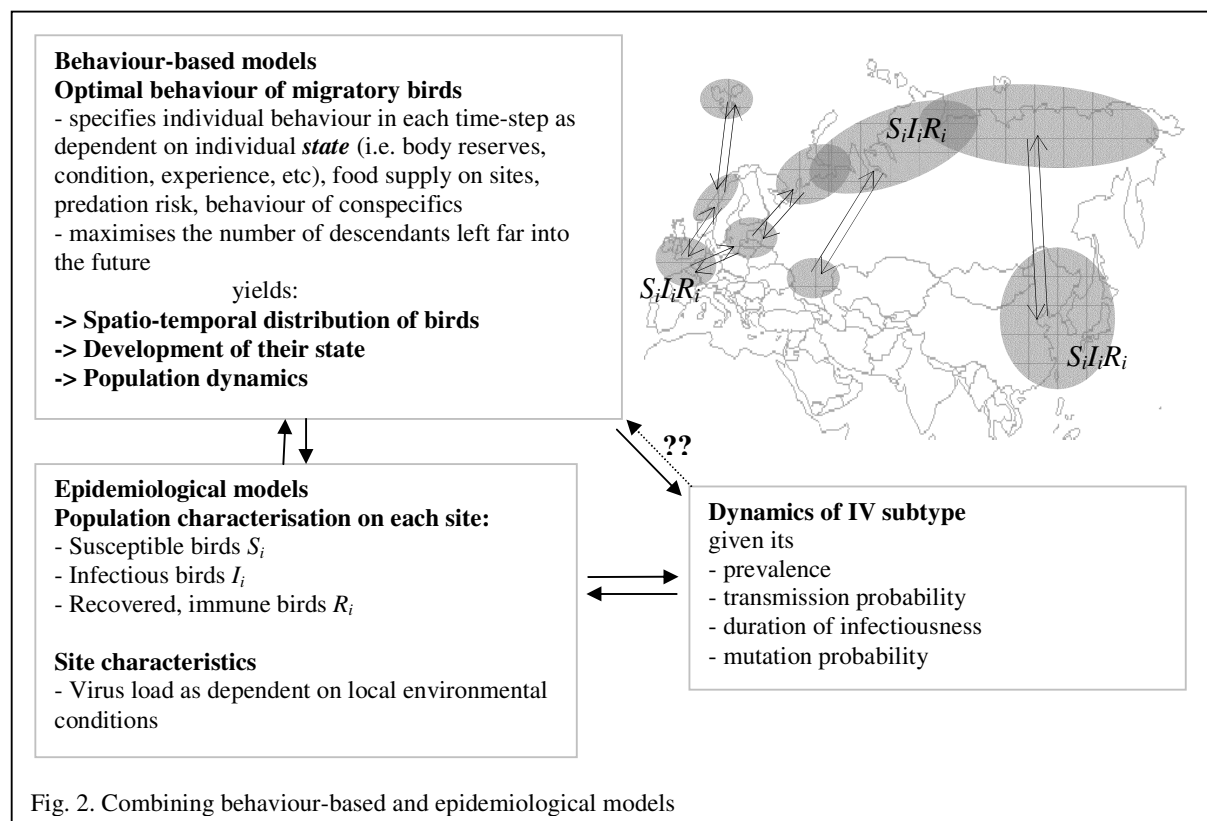


Fig. 2. Combining behaviour-based and epidemiological models

## 2. Epidemiological models

Epidemiological models have been used to promote an understanding of the reassortment in the influenza virus and the spread of subtypes. No work has yet been done targeting the migration of waterfowl. In effect, we are dealing with a particular type of metapopulation where the individuals collectively move between one (set of) location(s) (breeding grounds) to another (wintering grounds), mixing in moulting and stopover areas along the route. Mechanistic epidemiological models will be used to investigate under which conditions and assumptions the virus can persist (even a single type) in such a system. We will do this by incorporating the possible within-host effects of the virus on migration success. In this way, we can investigate the consequences of these effects on the between-host spread of the virus in the complete migratory cycle.

We will develop epidemiological models, which successively increase in complexity. The first – or null-model will be a metapopulation model with an implicit spatial structure, i.e. we consider wintering, breeding and stop-over sites without further spatial resolution (see Figure 2). Conditions on all sites will be specified with



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regard to the virus reservoir, i.e. subtype, virus load, and its temporal dynamics. Thus, we specify characteristics of the environment that have been identified to affect the persistence of IV until potential re-infections in later times, e.g. availability and temperature of freshwater bodies.

The bird population is characterised as follows – the number of non-infected, susceptible individuals  $S$ , the number of infectious individuals  $I$ , and the number of recovered individuals  $R$  that have gained immunity against the present virus type. The distribution of birds over SIR on a given site in the migration chain is determined by the “final” conditions on the previous site. On each site, the disease is transmitted according to the local conditions and to the number of birds present. The dynamics of movement between sites (i.e. what “final” is in each separate site) is determined by the behaviour-based processes outlined above in the combination step 3 below. The basic local epidemiological model will be adapted when necessary (e.g. latency phase, environmental reservoir).

The further development of the disease, i.e. the transition from  $S \rightarrow I \rightarrow R$ , depends on the characteristics of the particular sub-type of IV, its latency, infectious period and immunity. Furthermore, dependent on the severity of the disease, infected birds will suffer a particular mortality.

In this framework we will identify the conditions under which the virus can persist. In particular, we will test the range of the following parameters with regard to the dynamics of IV types: impact on fitness-relevant processes in individual birds, the individual consequences of immune response to infections, transmission probability (between individuals), duration of infectiousness, level of immunity, and mutation probability of the virus type.

### 3. Link bird migration and epidemiological models

In the last step, we will combine our knowledge gained from both modelling studies and empirical results (see companion proposal) to develop a behaviour-based model for bird migration, which explicitly considers the infection status in a bird's state and consequently, allows the bird to incorporate infections in its decisions. Thus, the optimal behaviour of a bird will depend also on the dynamics and characteristics of the particular IV subtype.

### Innovative aspects

The tremendous biocomplexity of disease problems implies that a multidisciplinary approach is our best hope of smart combat strategies. Despite the obvious need for an integrative approach in these matters (Fouchier et al., 2005b), there are currently few research efforts in the world that tackle the risk assessment for influenza outbreaks as in the here proposed multidisciplinary fashion.

The research project cannot be conducted by any of the research partners in isolation. For the collection of samples, the virologists rely on the waterfowl ecologists. For tuning their program towards the right areas, times of the year, and species, the waterfowl ecologists need to rely on the IV screening by the virologists, but can only do so after consulting epidemiologists with their experience in population dynamics in viruses. Ultimately, the ecological data from waterfowl and data on IV prevalence and genetics will feed into the epidemiological models. Never before have epidemiological and behaviour-based models been combined to investigate the ecology of an infectious diseases in natural populations (Hudson et al, 2002). For the ecology of IV we think it is an essential advance.

Within the NIOO various projects exist on the population dynamics, migratory behaviour (Beekman et al. 2002; Klaassen et al. 2005) and habitat use (Beekman et al. 2002; Klaassen et al. 2005; Nolet et al. 2002) of waterfowl, among others in relation to global and regional change.

Researchers at the Department of Theoretical Epidemiology-UU, have been involved in the epidemiological modelling of infectious diseases and are experienced in a wide variety of mathematical modelling techniques to describe the impact of contact patterns on the spread of infectious diseases (Diekmann & Heesterbeek, 2000).

The large gene database on IV that is present at the dept. of Virology-EMC and the insight on species of interest and the biology of IV will be essential for the studies proposed here.

Thus, each of the three research groups is well established in their respective fields and has ongoing international collaborations in their specific area of expertise. Through this proposed collaboration, each of the groups will get access to the networks of the three areas of expertise, thereby strengthening their positions for the future, even beyond this 3-year project. The knowledge, data and methods brought to this project by the participants are a unique combination, coming together for the first time.





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### 5. Timetable of the project and working programme:

	2006		2007				2008				2009					
	Sum	Aut	Win	Spr	Sum	Aut	Win	Spr	Sum	Aut	Win	Spr	Sum	Aut		
<b>Epidemiological models</b>																
1. Null-model development and analysis	█															
2. Metapopulation model			█													
3. Sensitivity analyses					█		█									
<b>Behaviour-based models</b>																
1. Model adjustment			█													
2. Parameterisation for target waterfowl					█											
3. Sensitivity analyses							█									
<b>Linked models</b>																
Model adjustment									█							
Parameterisation & Analysis											█		█			
<b>Publications</b>																
			█						█						█	

### 6. Affiliation with (inter)national research programmes

(This should include an explicit description of existing and planned cooperation)

At the moment the group of theoretical and infectious disease epidemiologists at FVM participates in several FP 6 EU projects (with two PhD students and two postdocs) relevant to the present proposal. One involves Avian Influenza (a thorough analysis of the Dutch outbreak of H7N7 and the outbreak of H5N1 in Thailand), the other two are from the theoretical side and involve emerging infections: i) EDEN (Emerging Diseases in a changing European eNvironment), this is an IP with more than 30 partners, where J.A.P.H. is in the Steering Committee and FVM is the partner coordinating the modeling work in the project as a whole; ii) SARSTRANS, this is a small project with only three European partners, led by the group of R.M. Anderson at Imperial College, London, and partners in the Far East, where FVM takes the lead in methods to estimate control effort needed and the usefulness of contact tracing. J.A.P. H. was awarded a VICI grant by ZonMw/NWO at the end of 2004, titled: Population dynamics and control of infectious diseases: modeling interaction at different scales. The EDEN project could provide particularly relevant additions to the present proposal as it deals with effects of climate change on emerging infections.

For the screening of waterfowl for IV prevalence a network of researchers is required. NIOO/UU can rely on an extensive network of collaboration on these groups of birds. For instance NIOO/UU has (inter)national co-operations running on a number of potential target species including Bewick's Swans (with Dutch partners T. Haitjema and J. H. Beekman, and the British Wildfowl and Wetland Trust [Dr. E. Rees]), Pink-footed Goose (Danish National Environmental Research Institute [Dr. J. Madsen]) and Barnacle Goose (RUG [G. Eichhorn] and the British Wildfowl and Wetland Trust [Dr. E. Rees]). Currently NIOO is co-operating with WWT and NERI in the framework of the 6<sup>th</sup> framework EU project "fragility of Arctic goose habitat: impacts of land use, conservation and elevated temperatures (FRAGILE)". Within this project NIOO models the long-distance migratory behaviour and population dynamics of PFG and Barnacle Goose.

With WWT and the two Dutch initiators of Bewick's Swan ringing schemes NIOO has recently embarked on a KNAW funded Avian Spatial Ecology co-operation which focuses on describing and modelling small scale spatial dynamics of Bewick's Swans. Additionally, NIOO co-operates with NERI on the breeding grounds of Pink-footed Goose (Spitsbergen). In the past NIOO has organised expeditions to the Russian breeding grounds of Bewick's Swans. An enterprise that we are intending to pick up in co-operation with WWT has continued to go there over the past years.

Besides these projects covering the complete flyways of the three species mentioned, NIOO has numerous other waterfowl contacts that will be especially of relevance for the initial broad scale surveillance.

The dept. Virology at EMC houses the Dutch WHO national influenza centre. EMC is coordinator of the EU framework 5 programme "NovaFlu", in which novel vaccine candidates for pandemic IVs are designed and tested. One of Dr. Fouchier's activities in this programme is the generation of an avian IV database. In this programme, avian samples are collected through a large international network of ornithologists. IVs collected within the context of this application will be added to the existing databases. After 2005, the database FP5



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project will be continued in the NWO/WOTRO programme “Nivarec”. As a fellow of the Royal Dutch Academy of Arts and Sciences from 2000-2005, Dr. Fouchier developed new methods to study determinants of IV zoonosis and pathogenesis, which will be invaluable for the current proposal. Fouchier is also one of 19 partners in the framework 6 programme coordinated action RiViGene (Risk Virus Gene database), for which Dr. Fouchier will generate and maintain genetic data on avian IVs. The genetic data from IV isolates in the current proposal will be compared with available datasets, and correlated with biological properties of the IVs. Virus isolates of subtypes H5 and H7 will be sent to the Central Institute for Animal Disease Control (CIDC; Dr. G. Koch), to test for pathogenicity in chickens, according to EU laws. Virus characteristics (genetic of phenotypic) will be implemented in the epidemiological models.

**7. Societal significance**

Motivation of the relevant policy aspects, such as:

- Political / societal significance in a national and international context
- Urgency for international and/or national policy

(These are important for the evaluation of the proposal, because of the funding by several ministries.)

Influenza outbreaks form a major threat to human health and economy. Waterfowl is thought to be among the most important reservoirs and vectors of transport for influenza viruses. With its dense human population, extensive pig and chicken farming, its many shallow water bodies, which attract migratory waterfowl in unparalleled numbers, The Netherlands form a hot spot for the development of new pandemic influenza outbreaks. The rapidly increasing numbers of outdoor ranging poultry and pigs further increase the risks in The Netherlands. For risk reduction, early recognition and management of outbreaks now and in the future, the proposed multidisciplinary research initiative will provide critical knowledge on the prevalence of influenza viruses in waterfowl and their potential to evolve to virulent viruses for humans. Our results will be invaluable for the discussions on the risk-management of avian IVs with respect to transmission to poultry, animals and humans in Europe.

**8. Legal requirements**

For fieldwork to Antarctica additional information is needed for an initial assessment whether or not the applicant will have to apply for a permit under the ‘Wet bescherming Antarctica’.

Do you plan to visit Antarctica, South of 60°S?  No

If the above question is answered with “yes” please fill in the separate ‘WBA-IPY’ form for details

Has been complied with the law and legal requirements with respect to the proposed Research, such as ‘Wet op Dierproeven’ and ‘DNA-recombinant legislation?’

Yes

**9a. Requested budget from ALW**

	2006	2007	2008	2009	2010
Personnel (mm)	6	12	12	6	
Research costs (k€)					
Equipment	7.5				
Consumables	2.5	2.5	2.5	2.5	
Fieldwork					
Education, Outreach & Communication					
Coordination*					
Shiptime NIOZ-MRF (in days)					



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(IPY•NL)**



\* Costs for coordination can only be requested if main applicant is lead contact of the related IPY "Full proposal". If this is a subproject of a coordinating project proposal, the coordination costs can only be requested in the application form of the coordinating project.

**9b. Explanation and/or remarks to the proposed budget:**

(Personell, equipment, consumables, fieldwork, EOC, coordination and Shiptime NIOZ-MRF)  
(Education, Outreach & Communication (EOC) plan must be included here)

a. Proposed personnel (please note that, unless your preliminary proposal deals with a multidisciplinary project involving at least 2 of the 3 research themes within this programme, you may not request more than 1 full person equivalent, f.t.e.)

1 Post-doc researcher.

b. Estimated research costs (durables+consumables+travel) (€):

- multi-processor pc for high computational requirements (7500 €)
- scientific conferences (2 per year) and regular visits to project-partners (2500 € per year)

c. Estimated costs of joint activities (€):

d. If applicable, indicate the approximate amount and source of additional funding to be sought:

(€): 0 from: ---

**10. Financial assistance from (an)other source(s)**

None.

**11. Relation research program university, large institutions, research schools, etc.**

This project fits very well in the new research programme *Strategic Infection Biology* (2006-2011) of the FVM, where viral infections, and notably viral zoonoses, are a prime focus of study over many interacting levels of biological organisation (from molecular to population). As part of the research programme the work also fits very well into the VICI project of the main applicant. This VICI project is titled *Population dynamics and control of infectious diseases: modelling interaction at different scales* (2005-2010). That project focuses on the interaction between processes in infectious disease spread that inherently deal with more than one level of biological integration. In the present proposal this translates as the fundamental interaction between local mixing (breeding grounds/resting grounds/winter habitat) and global mixing.

(No signatures required for electronic submission)