

# Infect

## Modelling spread of infectious diseases in fish farming

**Innovation area:** Marine

**Key Innovator:** Magne Aldrin

**Partners:** UiO, NR, HI, National Veterinary Institute

**Research staff scientists:**

Magne Aldrin (NR, principle investigator), Bård Storvik (NR), Ragnar Bang Huseby (NR), Anders Løland (NR), Arnoldo Frigessi (UiO), Odd Aalen (UiO), Ørnulf Borgan (UiO), Birgitte de Blasio (UiO, principle investigator), Peder A. Jansen (Norwegian Veterinary Institute), Hildegunn Viljugrein (Norwegian Veterinary Institute), Gianpaolo Scalia Tomba (Roma II), Trude Lyngstad (Norwegian Veterinary Institute), Anja Bråthen Kristoffersen, (Norwegian Veterinary Institute), Lars Asplin (HI), Vidar Aspehaug (Patogen Analyse AS), Magnus Devold (Patogen Analyse AS), Audun Stien (Norwegian Institute for Nature Research), Randi Grøntvedt (Norwegian Veterinary Institute)

**Additional reference group:** Gordon Ritchie (Marine Harvest), Olav Breck (Marine Harvest)

**International contacts and collaborators:** Gianpaolo Scalia Tomba (University of Rome II, Italy), National Veterinary Institute (Denmark), Agence nationale de securite sanitaire (France), Froedrich Loeffler Institut (Germany), Institut francais de recherché pour l'exploitation de la mere (France), Intitut des Sciences de l'Evolution de Montpellier (France), Fredrik Liljeros (Stockholm University), Bjørn Iversen (Norwegian Institute of Public Health)

### Scope:

Design stochastic models for the spread of infectious diseases between fish farms, and use the model to improve management strategies in the fish farming industry.

Stochastic network models for the understanding and management of human infectious diseases.

### Results in 2012 and plans:

*Marine epidemiology*

#### **1. Molecular Tracing of Viral Pathogens in Aquaculture (MOLTRAQ) - Scenario simulation models for control options (Ongoing European project)**

Our part of this project is dedicated to developing generic modelling tools for exploring effects of different intervention strategies on the incidence of disease outbreaks in aquaculture enterprises. The modelling tools will be based on a stochastic, spatio-temporal model developed for the spread of infectious salmon anaemia in Norwegian salmon farming (Aldrin et al. 2011), which exploits both traditional epidemiological data and genetic data characterizing the disease agent. This model will be adapted to other host - pathogen systems incorporated in the present project, with a priority for systems where the total data from different sources are most complete. Even if pathways for the spread of pathogens between aquaculture stocks depend on both pathogen and host characteristics, the context is very much the same from a modelling

point of view. Farms are located at fixed coordinates, distances (seaway) between farms play an important role, networks representing commercial trade or local contact are relevant, and characteristics of the farms (water temperature, biomass, number of fish) are important. The models will be used to investigate different intervention strategies to reduce the number of disease outbreaks in the future, using numeric simulations of disease spread under various scenarios. Interventions such as progressed culling of infected farm stocks, neighbourhood surveillance and culling, or vaccination, are topics of interest to explore.

## ***2. Space-time modelling of sea lice population dynamics in aquaculture - farm-level population models and regional transmission dynamics (proposal submitted to the Research Council of Norway)***

The development and analysis of biologically realistic mathematical models has revolutionised our understanding of infectious disease dynamics and become a main tool in the design of efficient management strategies for infectious diseases. The epidemiological theory for the spatio-temporal dynamics of many viral, bacterial and protozoan diseases of humans and livestock is now well developed. The epidemiological theory of metazoan parasites and the statistical methods available for analysing the spatial-temporal dynamics of such diseases are, however, less developed. An important reason for this situation is that the more complicated life histories of this group of infectious organisms require more advanced modelling. An additional reason may be that relevant high resolution spatio-temporal data on host-metazoan parasites systems are hard to come by. This research proposal will contribute new methods for the analysis of the spatio-temporal dynamics of metazoan parasites. More specifically we will construct a biologically realistic stochastic stage structured model for the population dynamics of salmon lice in the Norwegian transmission network of marine salmon farms. The full model is a Bayesian hierarchical model which includes: i) a stage structured population model for salmon lice on individual salmon farms, ii) a model for within-farm transmission of lice, and iii) a model for the between-farm transmission of lice, where seaway distances between farms play a prominent role. The model parameters will be estimated based on experimental data and from more than ten years of full scale field data from all Norwegian salmon farms. Finally, we will demonstrate how the model can be used to guide management strategies for sea lice control.

## ***3. Simulation modelling of the spread of pancreas disease in salmon farming: effects of various control regimes (proposal submitted to the Research Council of Norway)***

Pancreas disease (PD) is arguably the most important disease in Norwegian salmon farming in recent years. High incidence rates of PD outbreaks in marine salmon farms, large economic losses and a control-legislation under intense debate all testify to the importance of this disease. In order to effectively control the spread of PD, it is essential with knowledge on the pathways of transmission of the aetiological salmonid alphavirus (SAV) and the extent of interruption of such transmission through different protective actions. Data-driven statistical models have proven useful in quantifying the space-time spread of PD in Norwegian salmon farming through different pathways of transmission. The present proposal aims to further develop these models into simulation models that can be used as a mathematical laboratory in testing effects of different protective actions. The output of the simulation modelling will be likely incidence rates of PD outbreaks and likely geographical distributions of outbreaks under different control scenarios. Economic analyses of costs and benefits relative to different scenarios will be undertaken, based on the simulation outputs

The 2009 A(H1N1) influenza pandemic was the first pandemic where vaccines and antivirals were available. It is therefore important to evaluate the effectiveness of timing of these intervention measures. In Norway, vaccination commenced in week 43 during the major pandemic outbreak and reached a 40% population coverage. During the pandemic, Norwegian pharmacists were allowed to issue prescription of antivirals to ease pressure on health care services. We developed an age-structured SEIR model using data on vaccinations and sales of antivirals in 2009/10 in Norway, and fitted the model to Norwegian influenza-like-illness (ILI) data. Our results indicate that vaccination came too late to have a strong influence on the pandemic in Norway and that the countermeasures prevented approximately 11–12% of potential cases relative to an unmitigated pandemic. Vaccination was found responsible for roughly 3 in 4 of the avoided infections. An estimated 50% reduction in the clinical attack rate would have resulted from vaccination alone, had the campaign started 6 weeks earlier. Had vaccination been prioritized for children first, the intervention should have commenced approximately 5 weeks earlier in order to achieve the same 50% reduction. In comparison, we estimate that a non-adjuvanted vaccination program should have started 8 weeks earlier to lower the clinical attack rate by 50%. In conclusion, vaccination timing was a critical factor in relation to the spread of the 2009 A(H1N1) influenza. Our results also corroborate the central role of children for the transmission of A(H1N1) pandemic influenza.

Internet dating has become increasingly popular and a socially acceptable way to meet partners for dates and relationships. Online dating has the ability to transcend social and geographic barriers, which may have an impact on sexual contact networks and influenza transmission patterns of sexually transmitted infections (STIs). To improve our understanding of these new social media-based interactions, it is important to explore, describe and characterize their network properties. We analyzed a 2 months data log of flirt messages expressing sexual interest among men who have sex with men (MSM) within the online *Qruiser.com* community. We examined the characteristics of MSM sending and receiving flirt messages and their individual activity and popularity on the site. In addition we analyzed the structural properties, including the core structure of the flirt network. MSM were more likely to send flirt messages if they were homosexual and aged 40+ years while young people aged < 30 years were more likely to receive a flirt. Central members in the flirt network were more likely homosexuals, singles and aged 31-40 years. The flirt network showed high degree heterogeneity similar to the structural properties of real sexual contact networks. Interestingly, we observed a single central core in the network surrounded by several disjunct non-central cores that only can be reached through the central core. This finding is likely to enhance importance of the core for disease transmission and highlights its importance for potential strategic interventions.

More generally, sexual contact networks are characterized by a highly uneven distribution in contact numbers: most people have very few sex partners during their lifetime while a minority of people has very many partners. The tail of the sex partner distribution has been found to exhibit scaling behavior, and is often modeled by a simple power law. Preferential attachment is a popular generative mechanism to explain the widespread observation of power-law in the natural and social science. Preferential attachment is a stochastic growth process where the probability for individuals to make new contacts is an increasing function of the number of connections they have. An alternative, but much less studied explanation for the phenomenon is a randomly grown network with large individual variation in growth rates among the nodes (frailty). We derive analytically the distribution of individual rates, which will reproduce the connectivity distribution that is obtained from a general preferential attachment process (Yule process), and the structural differences between the two types of graphs are examined by simulations. We present a statistical test to distinguish the two generative mechanisms from each other and we apply the test to both simulated data and two real data sets of scientific citation and sexual partner networks. The findings from the latter analyses argue for frailty effects as an important mechanism underlying the dynamics of complex networks.

## Papers:

Aldrin, Magne; Lyngstad, Trude Marie; Kristoffersen, Anja Bråthen; Storvik, Bård; Borgan, Ørnulf; Jansen, Peder Andreas: Modelling the spread of infectious salmon anaemia (ISA) among salmon farms based on seaway distances between farms and genetic relationships between infectious salmon anaemia virus isolates. *Journal of the Royal Society Interface*, 2011; Vol. 8(62): 1346-1356.

Aldrin, M; Raastad, R; Tvette, IF; Berild, D; Frigessi, A; Leegaard, T; Monnet, DL; Walberg, M; Müller, F. Antibiotic resistance in hospitals: a ward specific random effect model in a low antibiotic consumption environment. *Statistics in Medicine*, 2012; doi: 10.1002/sim.5636.

Aldrin, M., Storvik, B., Frigessi, A., Viljugrein, H. and Jansen, P. A.: A stochastic model for the assessment of the transmission pathways of heart and skeleton muscle inflammation, pancreas disease and infectious salmon anaemia in marine fish farms in Norway. *Preventive Veterinary Medicine*, 2010; Vol. 93: 51-61.

Berild, Dag; Abrahamsen, Tore G.; Andresen, Stein; Bjørnløw, Egil; Haug, Ola; Kossenko, Irina M.; Kubar, Olga I.; Lelek, Michaela; Mintchenko, Svetlana I.; Pyasetskaya, Maria F.; Ringertz, Signe H.; Sysenko, Galina A.: A controlled intervention study to improve antibiotic use in a Russian pediatric hospital *International Journal of Antimicrobial Agents*, Elsevier, 2008; Vol. 31(5): 478-483.

de Blasio B., Kasymbekova K., Flem E: Dynamic model of rotavirus transmission and the impact of rotavirus vaccination in Kyrgyzstan, *Vaccine*, 2010; Vol. 28(50): 7923-7932.

de Blasio, BF; Iversen, BG; Scalia Tomba, G. Effect of Vaccines and Antivirals during the Major 2009 A(H1N1) Pandemic Wave in Norway – And the Influence of Vaccination Timing. *PLoS ONE*, 2012; Vol. 7(1): e30018.

de Blasio, BF; Rae Neilson, A; Klemp, M; Skjeldestad, FE. Modeling the impact of screening policy and screening compliance on incidence and mortality of cervical cancer in the post-HPV vaccination era. *Journal of Public Health*, 2012; Vol. 34(4): 539-547.

de Blasio, BF, Seierstad TG, Aalen, OO: Frailty effects in networks: comparison and identification of individual heterogeneity versus preferential attachment in evolving networks. *J. Roy. Stat. Soc. C*, 2011; Vol. 60(2): 239–259.

Cori, A; Valleron, AJ; Carrat, F; Tomba, GS; Thomas, G. Estimating Influenza Latency and Infectious Period Durations using Viral Excretion Data. *Epidemics*, 2012; Vol. 4 (3): 132-138.

Gran, Jon Michael; Røysland, Kjetil; Wolbers, Marcel; Didelez, Vanessa; Sterne, Jonathan AC; Ledergerber, Bruno; Furrer, Hansjakob; von Wyl, Viktor; Aalen, Odd O: A sequential Cox approach for estimating the causal effect of treatment in the presence of time-dependent confounding applied to data from the Swiss HIV Cohort Study. *Statistics in Medicine* 2010; Vol. 29(26): 2757-2768.

Gran, Jon Michael; Iversen, Bjørn Gunnar; Hungnes, Olav; Aalen, Odd O: Estimating influenza-related excess mortality and reproduction numbers for seasonal influenza in Norway, 1975-2004. *Epidemiology and Infection*, 2010; Vol. 138(11): 1559-1568.

Jansen, PA; Kristoffersen, AB; Viljugrein, H; Jimenez, DD; Stien, A; Aldrin, M. Sea lice as a density-dependent constraint to salmonid farming. *Proceedings of the Royal Society of London. Biological Sciences*, 2012; Vol. 27(1737): 2330-2338.

Lavine, JS; Bjørnstad, ON; de Blasio, BF; Storsaeter, J. Short-lived immunity against pertussis, age-specific routes of transmission, and the utility of a teenage booster vaccine. *Vaccine*, 2012; Vol. 30(3), 544-551.

Pitzer, VE; Atkins, KE; de Blasio, BF; Van Effelterre, T; Atchison, CJ; et al. Direct and Indirect Effects of Rotavirus Vaccination: Comparing Predictions from Transmission Dynamic Models. *PLoS ONE*, 2012; Vol. 7(8): e42320.

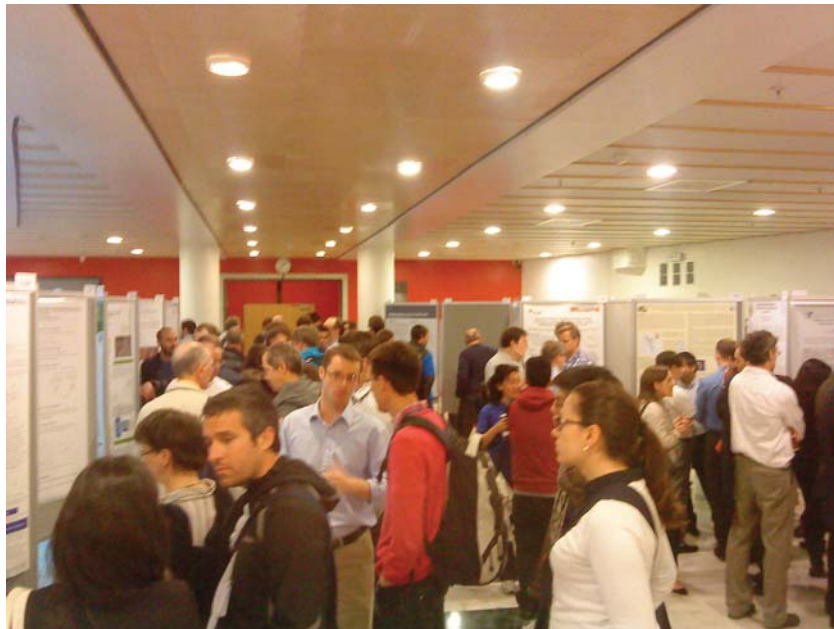
Scheel, I., Aldrin, M., Frigessi, A., Jansen, P.A.: A stochastic model for infectious salmon anaemia (ISA) in Atlantic salmon farming. *J. of the Royal Society Interface*, 2007; Vol. 4: 699-706.

Villani, A; Frigessi, A; Liljeros, F; Nordvik, MK; de Blasio, BF. A Characterization of Internet Dating Network Structures among Nordic Men Who Have Sex with Men. *PLoS ONE*, 2012; Vol. 7(7): e39717.

Xue, Yiting; Kristiansen, Ivar Sønbo; De Blasio, Birgitte: Modeling the cost of influenza: the impact of missing costs of unreported complications and sick leave. *BMC Public Health*, 2010; Vol. 10:724.

Xue, Y; Kristiansen, IS; de Blasio, BF. Dynamic modelling of costs and health consequences of school closure during an influenza pandemic. *BMC Public Health*, 2012; Vol. 12:962.

Zechmeister I., De Blasio, B., Garnett G: HPV-vaccination for the prevention of cervical cancer in Austria: a model based long-term prognosis of cancer epidemiology. *Journal of Public Health*, 2010; Vol. 18: 3-13.



Geostats 2012, UiO