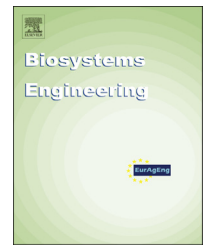


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Research Paper

Modelling seasonal and multi-annual variation in bank vole populations and nephropathia epidemica



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Nephropathia epidemica (NE) is a human infection caused by *Puumala virus* (PUUV), which is naturally carried and shed by bank voles (*Myodes glareolus*).

The objective was to develop a dynamic model of the NE cases and the bank vole population in both Finland and Belgium by defining the periodic components with a dynamic harmonic regression (DHR) model. The defined periodic components can be further used to adapt mechanistic Susceptible and Infective (SI) models regionally.

Despite the difference in bank vole population dynamics and NE cases between the Western European temperate zone and boreal zones the DHR model was able to quantify the dynamics of NE cases in Belgium and Central Finland with a coefficient of determination (R^2) of 0.70 and 0.82 respectively and to quantify the dynamics of bank vole population in Belgium and Central Finland with R^2 of 0.80 and 0.98 respectively.

DHR identified 18 month cycles in the bank vole population in Belgium. This approach demonstrated two year cycles in Belgian NE outbreaks. DHR identified three year cycles in Finnish bank vole populations which in turn cause three year cycles in the NE outbreaks in Central Finland. Because the bank vole population data in Finland was contemporary with

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the data of NE cases, the DHR showed a three month delay between the NE cases and the bank vole population in Central Finland.

This approach may help us in our understanding of the spatial and temporal dynamics of NE cases and the bank vole populations in different regions.

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Nomenclature

Bank vole dynamics

S	susceptible vole density, vole ha^{-1}
I_n	newly infected vole density, vole ha^{-1}
I_c	chronically infected vole density, vole ha^{-1}
P	overall density of the vole population, i.e. $S + I_n + I_c$, vole ha^{-1}
$b(t)$	birth rate at time t , y^{-1}
m	natural mortality rate, y^{-1}
$k(t)$	induced density-dependent effect and seasonal variation on mortality rates, $\text{ha y}^{-1} \text{vole}^{-1}$
$K(t)$	carrying capacity, vole ha^{-1}

Cyclical and seasonal models

$Y(t)$	Model output depending on the model (NE cases, vole ha^{-1})
$Q(t)$	sustained cyclical or quasi-cyclical component
$L(t)$	trend or low frequency component
$\alpha_i(t)$	stochastic time variable parameters
$\beta_i(t)$	stochastic time variable parameters
f_i	the frequencies associated with the (normally longer period) cyclical component radians month^{-1}
$\eta_i(t)$	the zero mean, white noise input

1. Introduction

Hantaviruses are rodent- or insectivore-borne viruses and some of them are recognised as causes of human haemorrhagic fever with renal syndrome (HFRS). Puumala virus (PUUV) is one of the hantaviruses which are transmitted to humans by infected rodents. The bank vole (*Myodes glareolus*) is the natural host of PUUV in vast areas of Europe. PUUV causes a general mild form of haemorrhagic fever with renal syndrome called nephropathia epidemica (NE) (Clement, Maes, & Van Ranst, 2006).

Mechanistic models play an important role in analysing the spread and control of infectious diseases in general (e.g. Anderson et al., 1979; May & Anderson, 1979) and many attempts have been made to build mathematical models describing the dynamics of bank vole populations and the spread and survival of PUUV (Allen, Langlais, & Phillips, 2003; Sauvage, Langlais, & Pontier, 2007; Sauvage, Langlais, Yoccoz, & Pontier, 2003; Wolf, Sauvage, Pontier, & Langlais, 2006). More specifically, these mechanistic models were built based on knowledge of different components such as an epidemiological compartment structure, the nature of the incidence, a demographical structure of the population, the interaction

between the demographical structure and the epidemiological incidence of the disease.

The transmission dynamics of PUUV, however, are very complex. They involve the interaction between environment, tree biology, the bank vole population cycles and human risk behaviour (Bennet et al., 2006). Consequently, mechanistic Susceptible and Infective (SI) models describing these complex interactions turn out to be complicated although they are still idealisations of reality which is much more complex than implied by the simplifying equations. In order to apply such models in practice (e.g. for prediction of disease outbreaks) the most important model parameters that are describing the dominant processes should be calibrated according to the considered application in real time. Thus, there is a need for updating such SI models under specific regional conditions. These mechanistic models can be compared against data-based mathematical procedures, where the model is inferred and the model parameters are directly estimated from experimental data using more objective statistically-based methods (e.g. Costa, Borgonovo, Leroy, Berckmans, & Guarino, 2009; Ferentinos & Albright, 2003; Rastetter, 1987; Thanh, Vranken, Van Brecht, & Berckmans, 2007; Ushada & Murase, 2006).

This paper considers a data-based mechanistic modelling approach (DBM) that is a hybrid between data-based modelling on the one hand and a mechanistic SI model on the other. DBM offers the advantage that it combines mechanistic process knowledge with measured information (e.g. NE cases and/or bank vole population time series) which makes them understandable from a biological/ecological point of view, but at the same time allows the model to take into account real-time measured information (temporal as well as regional) in order to predict the dynamics of NE outbreaks and bank vole population. Such model predictions could be used as a basis for an early warning monitoring system for NE outbreaks and bank vole population estimations.

The bank vole population dynamics and NE cases show multi-annual and seasonal as well as spatial fluctuations. We hypothesised that defining the periodic components of the NE cases and bank vole population dynamics may allow mechanistic SI models such as the Sauvage et al. (2003, 2007) model to be adapted for more specific regional circumstances.

In this study we aimed to show the ability of our approach to quantify the seasonal and cyclic components of the NE cases and bank vole populations in two different regions. Because of the difference between the Western European temperate zone and boreal zones biotypes, we used time-series data sets from Finland and Belgium. Furthermore, the research aimed to use the results of the dynamic harmonic regression (DHR) approach to adapt the Sauvage et al. (2007) model regionally by

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