Using singular perturbations to reduce an epidemiological model: Application to bovine viral diarrhoea virus within-herd spread

Sébastien Gaucel [a,*,1], Béatrice Laroche [b,c,d], Pauline Ezanno [e,f], Elisabeta Vergu [a], Suzanne Touzeau [a]

[a] *INRA, UR341 Mathématiques et Informatique Appliquées, F-78350 Jouy-en-Josas, France*
[b] *Laboratoire des Signaux et Systèmes, Univ Paris-Sud, UMR8506, Gif-sur-Yvette F-91190, France*
[c] *CNRS, Gif-sur-Yvette F-91190, France*
[d] *SUPELEC, Gif-sur-Yvette F-91190, France*
[e] *INRA, UMR1300 Bio-agression, Épidémiologie et Analyse de Risque, F-44307 Nantes, France*
[f] *ENVN, UMR1300 Bio-agression, Epidémiologie, Analyse de Risque, F-44307 Nantes, France*

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ABSTRACT

Studying the spread of a pathogen in a managed metapopulation such as cattle herds in a geographical region often requires to take into account both the within- and between-herd transmission dynamics. This can lead to high-dimensional metapopulation systems resulting from the coupling of several within-herd transmission models. To tackle this problem, we aim in this paper at reducing the dimension of a tractable but realistic dynamical system reproducing the within-herd spread. The context chosen to illustrate our purpose is bovine viral diarrhoea virus (BVDV) transmission in a cattle herd structured in two age classes and several epidemiological states, including two infectious states (transiently and persistently infected). Different time scales, corresponding to the epidemiological and demographic processes, are identified which allow to build a reduced model. Singular perturbation technique is used to prove that, under some non-restrictive conditions on parameter values, the behaviour of the original system is quite accurately approximated by that of the reduced system. Simulations are also performed to corroborate the approximation quality. Our study illustrates the methodological interest of using singular perturbations to reduce model complexity. It also rigorously proves the biologically intuitive assumption that transiently infected individuals can be neglected in a homogeneous population, when capturing the global dynamics of BVDV spread.

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1. Introduction

Theoretical studies on population dynamics most often involve relatively complex models, due to the intrinsic complexity of the phenomena that are captured (biological, demographic, etc.), to their interactions, and to the state dimension. Such is the case when studying the spread of a pathogen at a regional scale in a managed metapopulation such as cattle herds, which often requires to take into account the within-herd transmission dynamics, as well as the between-herd dynamics within the region of interest. Management induces an heterogeneous contact structure which needs to be taken into account for moderately propagating pathogens. This can lead to high-dimensional

metapopulation systems resulting from the coupling of several similar local within-herd transmission models. An appropriate approach to tackle this problem is to reduce the dimension of an epidemiological model designed to study the spread of a disease in a managed herd.

A possible solution for reducing the complexity consists in taking advantage of the presence of several time scales in the system. Indeed, events can intrinsically occur at different velocities which allows, under stability assumptions on the fast dynamics (see Khalil, 1996 and Appendix B), to neglect rapid events and therefore to build a lower-dimensional model, that can be handled analytically and that is governed by the dynamics of the slow events. Several mathematical methods allowing such system reduction, as aggregation of variables and singular perturbation, have been developed. These methods were used in biological fields, mainly in ecology (Lenbury, 1996; Lett et al., 2003), but also in epidemic modelling (González-Guzmán and Naulin, 1994; Song et al., 2002). From the methodological point of view, the aggregation of variables, perfect or approximate (Iwasa et al., 1987, 1989) are by far the most frequently used. The method, revised in Auger and Bravo de la Parra (2000),

was first applied in the frame of ordinary differential equations (Auger and Roussarie, 1994; Auger and Poggiale, 1998) and then derived for partial differential equations (Auger and Roussarie, 1994; Bravo de la Parra et al., 2000) discrete dynamical systems (Bravo de la Parra et al., 1995; Sanz and Bravo de la Parra, 1999) or for stochastic frameworks (Sanz et al., 2003; Sanz and Bravo de la Parra, 2007). Several papers, studying dynamics of structured population models, have used the singular perturbation method (Arino et al., 1999; Song et al., 2002).

In this paper, we are interested in reducing the order of an epidemiological model designed to study the spread of a disease in a managed herd. We aim at using the dimensionally reduced form of the model for further studies in a metapopulation context. A reduced-order model is easier to manipulate and control and can therefore be coupled with other similar local models for studying the propagation at the between-herd scale. In order to achieve a trade-off between complexity and tractability, we chose to adapt a generic epidemiological model to a concrete situation: bovine viral diarrhoea virus (BVDV) epizootic dynamics within a managed herd through a simplified but realistic model.

BVDV virus is a pestivirus which does not survive in the environment. Hence, horizontal transmission mainly occurs by direct contacts with infected animals. It leads to transiently infected animals excreting low amounts of virus during a couple of weeks (Baker, 1987) before becoming immune. No clear and specific clinical signs are usually observed. However, if infection occurs during early or mid-pregnancy, it frequently generates embryonic and foetal deaths. For cows infected during mid-pregnancy that do not abort, vertical transmission is highly probable. These cows give birth to persistently infected (PI) calves (Hartley and Richards, 1988; Fray et al., 2000). PI animals excrete the virus during their whole life in a greater amount than transiently infected animals (Baker, 1987). PI dams always give birth to PI calves. PI animals have a higher lethality, with a half-life of 1 year (Houe, 1993). Consequently, the disease induces high economic losses, which is why several European countries are implementing control plans (Lindberg et al., 2006).

To model BVDV within-herd spread, a classical non-structured SIR (susceptible/infected/recovered) model is not adequate. Both vertical and horizontal transmissions should be considered as they lead to very different consequences. Transiently infected and PI animals cannot be regrouped in a single infectious status because their infectiousness and infection duration are drastically different. Hence, this herd structure should be considered when modelling BVDV spread. To date, several models have been developed to represent the spread of BVDV in a cattle herd; a review can be found in Viet et al. (2007). They generally aim at studying the effect of control measures and assessing efficiency. These models are usually complex models which integrate detailed herd dynamics and include most of current biological knowledge on BVDV transmission. Most often, this complexity renders their rigorous mathematical analysis impossible. Moreover, the metapopulation model generated by coupling several such models to study the between-herd transmission at a regional scale could be difficult to simulate. The model that we propose here, whilst simpler than such complex high-dimensional models, still preserves the main characteristics of BVDV spread. It takes into account the heterogeneities in transmission that require the introduction of different disease statuses. It represents a compromise between realistic complexity and mathematical tractability.

The paper is organised as follows: in Section 2, we first present the BVDV model, then we analyse its structural properties. Exploiting the different time scales in the system corresponding to different biological processes, reduced-order models are built using the singular perturbation approach (Khalil, 1996); we then check the accuracy of these time scale approximations by using appropriate theorems (Section 3). In order to illustrate our analytical results, simulations are presented using realistic parameter values (Section 4). Finally, we discuss the methodology and the biological interpretation of our findings (Section 5).

2. Epidemiological model

We present in this section a model describing BVDV dynamics in a cattle herd located in a region where the disease in endemic. Hence, neighbouring herds contribute to the herd contamination. Purchases however are considered to be safe, as we assume that tests are performed for each animal introduced in the herd.

The mathematical model is first presented. This model exhibits different time scales between the demographic and epidemiological processes which are then outlined. Finally, we investigate the model equilibria.

2.1. Model description

The herd is structured in two age classes: Class 1, formed by juveniles (0–3 years), which are animals before breeding; and Class 2 formed by adults (>3 years of age). This population structure is motivated by herd management, outflows, reproduction and entries in the herd depending on age.

In age class i, animals are classified into mutually exclusive BVDV health statuses (Fig. 1): susceptible (S_i), transiently infected
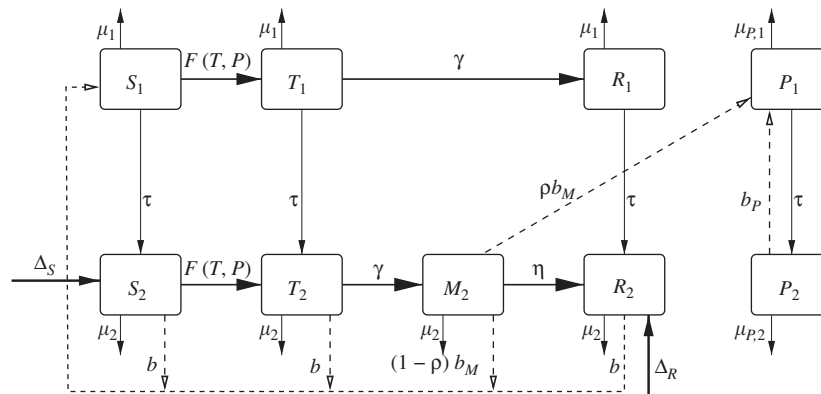

Fig. 1. Flow diagram of the epidemiological model representing BVDV health statuses per age classes and transitions between these states; in age class i, S_i: susceptible, T_i: transiently infected, P_i: persistently infected, R_i: recovered, M_2: recovered but still pregnant since infection. Parameters are defined in Table 1 and the model equations are given by (1).