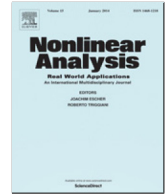




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## Nonlinear Analysis: Real World Applications

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## Modeling the spatiotemporal variations in brucellosis transmission

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## ARTICLE INFO

*Article history:*

Received 31 December 2016

Received in revised form 10 April 2017

Accepted 17 April 2017

*Keywords:*

Brucellosis

Spatial variation

Seasonal oscillation

Threshold dynamics

## ABSTRACT

In this paper, we propose a nonlinear modeling framework to investigate the transmission dynamics of brucellosis, incorporating both the spatial and seasonal variations. The spatial modeling is based on a patch structure, and the seasonal impact is represented by utilizing time-periodic model parameters. We demonstrate this framework through a two-patch model and conduct detailed analysis, for the cases with and without seasonal oscillations, respectively. In particular, we establish the threshold dynamics results using the reproduction numbers defined under different scenarios. Our findings underscore the importance of including spatial and seasonal heterogeneities in the design of control strategies for brucellosis.

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## 1. Introduction

Brucellosis, an infectious bacterial disease, is one of the world's major zoonoses. Caused by various species of the bacteria *Brucella* [1], the disease can be transmitted to animals and humans with exposure to infected animals or ingestion of contaminated water, food, and dust, etc. [2]. In animals, especially among sheep and goats, brucellosis mainly affects the reproduction process and can lead to fertility problems and abortion, and reduce the survival of newborns [3]. In humans, mortality is negligible, but the illness can last for several years [4], characterized by such symptoms as intermittent fever, headache, fatigue, joint and bone pain, psychosis, and disturbance [5].

Currently there are more than 500,000 new cases of brucellosis reported annually and the disease remains endemic in many areas of the world, including Spain, Latin America, the Middle East, and Africa [6,2]. Among these, the majority of brucellosis cases are found in sub-Saharan Africa, where Ethiopia, Chad, Tanzania, Nigeria, Uganda, Kenya, Zimbabwe and Somalia have been reporting persistence of brucellosis in humans attributed to the infection of domestic cattle, camels, goats and sheep [7]. With large pastoral

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communities, and the demand for meat and livestock products to double by 2050, brucellosis poses a major threat to the public health and economic growth of the region and demands serious control efforts.

Mathematical modeling, analysis and simulation offer a useful means to understand the transmission and spread of brucellosis so that effective disease control measures could be designed. A few mathematical models have been published in recent years to investigate brucellosis dynamics. For example, Ainseba et al. [8] constructed and analyzed a mathematical model for ovine brucellosis that incorporated direct, indirect and vertical transmission routes. Hou and co-workers [9] employed a system of ordinary differential equations (ODEs) to model the transmission of brucellosis and the effects of vaccination on brucellosis prevention and intervention. Lolika et al. [10] proposed a brucellosis model and conducted an optimal control study on the use of animal vaccination and environmental decontamination as disease control measures against brucellosis infection. Li et al. [11] proposed a model to investigate the transmission of brucellosis among sheep and from sheep to humans, and their findings indicated that a combination of intervention methods (such as prohibiting mixed feeding, vaccination, and detection and elimination) is useful in controlling human brucellosis.

Despite these efforts, however, several challenges remain in the mathematical modeling of brucellosis. First, different places likely have different geographic, ecological and environmental structures, and animals living in various locations likely exhibit different contact and communication patterns. In particular, animals make regular migration from one place to another, which directly contributes to the disease spread. So far these differences of the transmission dynamics have not been taken into account, leading to inadequate understanding of the influence of the spatial factors in the transmission and spread of brucellosis. Another limitation in brucellosis modeling is that the impact of seasonal variation is insufficiently addressed. In fact, like many other infectious diseases [12–14], brucellosis is significantly influenced by seasonal changes, and prior field studies have already demonstrated a strong correlation between brucellosis outbreaks and seasonal oscillations [15–17]. For example, a recent analysis of brucellosis datasets in a few countries [17] reveals that there is a marked seasonal variation in the incidence of acute brucellosis, with most cases occurring in the spring and summer. Factors such as periodic changes in temperature, seasonal precipitation which directly affects the availability of forage, environmental fluctuations in humidity and exposure to UV light which impact the survival of *Brucella*, and seasonal rituals in Africa which are associated with animal migration and slaughtering, all contribute to seasonal fluctuations in the transmission and spread of brucellosis.

Such spatial and temporal heterogeneities have strong impacts on the dynamics of brucellosis that are not captured by homogeneous, autonomous differential equation models. In the present study, we will make a first step toward integrating the spatial and seasonal variations into a single framework for a comprehensive modeling of brucellosis dynamics. To that end, we make use of the patch modeling approach (see, e.g., [18,19]) — we propose a two-patch deterministic model, where each patch has distinct populations and infection characteristics, to study the transmission of brucellosis among animals. In each patch, the animal population is subdivided into the susceptible and the infected compartments; meanwhile, another compartment is introduced to represent the concentration of the pathogen (i.e., *Brucella*) in the environment. Both the indirect (i.e., environment-to-host) and direct (i.e., host-to-host) transmission routes are considered in our model, representing the multiple pathways in the force of infection for brucellosis. Animals may move from one patch to the other, representing their migration in space. Additionally, we will incorporate the effects of seasonal oscillation by employing time-periodic model parameters, which leads to a non-autonomous patchy ODE system.

We organize the remainder of this paper as follows. In Section 2, we first introduce our two-patch model in the autonomous form, where each model parameter is fixed as a constant, and then conduct a thorough equilibrium analysis for this model. In Section 3, we extend the autonomous model to a periodic two-patch model and analyze the threshold dynamics. In Section 4, we use numerical simulation results to validate our analytical predictions. Finally, we conclude the paper with some discussion in Section 5.

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